Cancer Therapeutics Innovation Pipeline

Request for Applications
Early Validation and Early Accelerator proposals

Version 1.0

April 2024

OICR
Ontario Institute for Cancer Research

TABLE OF CONTENTS

1. INTRODUCTION

1.1. Purpose

This document is intended to aid Investigators wishing to apply for a Cancer Therapeutics Innovation Pipeline (CTIP) award to support the translation of Ontario discoveries into therapeutic assets with the potential for improving the lives of cancer patients. For more information on OICR and the Therapeutic Innovation research theme, please visit our website.

1.2. Cancer Therapeutics Innovation Pipeline (CTIP)

In 2017, OICR established the CTIP Program to capitalize on Ontario's expertise in cancer biology and drug discovery. Its aim is to create a pipeline of validated cancer targets and First-in-Class (FiC) or Best-in-Class (BiC), novel, selective lead molecules (small molecules or biologics) that will attract partnerships and/or investment for further preclinical and clinical development. To generate a sustainable pipeline, CTIP will support projects that aim to provide increasing evidence of target validation and disease association using data from knowledge bases, functional assays, and drug screening in relevant *in vitro* and *in vivo* models of the cancer type of interest.

CTIP funds projects in four stages of preclinical drug discovery as shown in Figure 1:

- **Early Validation (EV) projects:** Deliver robust translational evidence that a Target-of-Interest (TOI) is associated with a specific cancer type(s) based on data from knowledge bases and from studies demonstrating that perturbation of the TOI in relevant cell-based models produces anti-cancer effects sufficient to trigger a drug discovery campaign.
- **Early Accelerator (EA) projects**: Deliver a validated primary assay to enable initial screening of molecules against a defined target. Preliminary evidence of linearity of results between the primary assay and supporting secondary assays under development is also required. At the end of the EA stage, teams must demonstrate the capability and capacity to scale up production of reagents, recombinant proteins, and/or cell systems needed to support the medium-high throughput screening campaigns of the Late Accelerator stage.
- **Late Accelerator (LA) projects**: Focus on screening, using validated primary, secondary, and orthogonal assays and deliver confirmed Hit[1] molecules against a defined target supported by evidence of disease association. A confirmed Hit molecule should possess features that support its potential to become a Lead[2] molecule.
- **Lead Generation (LG) projects**: Deliver high-quality Lead molecules (small or large), with demonstrated *in vivo* efficacy, ideally accompanied by pharmacodynamic and/or efficacy biomarkers, and markers of resistance (where applicable), that correlate with target modulation. Lead molecule profiles should be sufficiently mature to attract partnership/investment for further development and ultimately commercialization. In addition, a clear path for development of defined biomarkers to guide patient selection is required together with a Target Product Profile (TPP[3]).

[1]A minimal definition of a Hit is a molecule series with an understood Structure-Activity Relationship (SAR) and selectivity profile in relevant *in vitro* models.
[2]A minimal definition of a Lead is a molecule series with an understood SAR and selectivity profile in pharmacologically relevant *in vivo* models.
[3]A TPP outlines the desired profile or characteristics of a drug that is aimed at a particular disease. In addition, a TPP states the intended use, target populations and other desired attributes of a drug, including safety and efficacy-related characteristics.

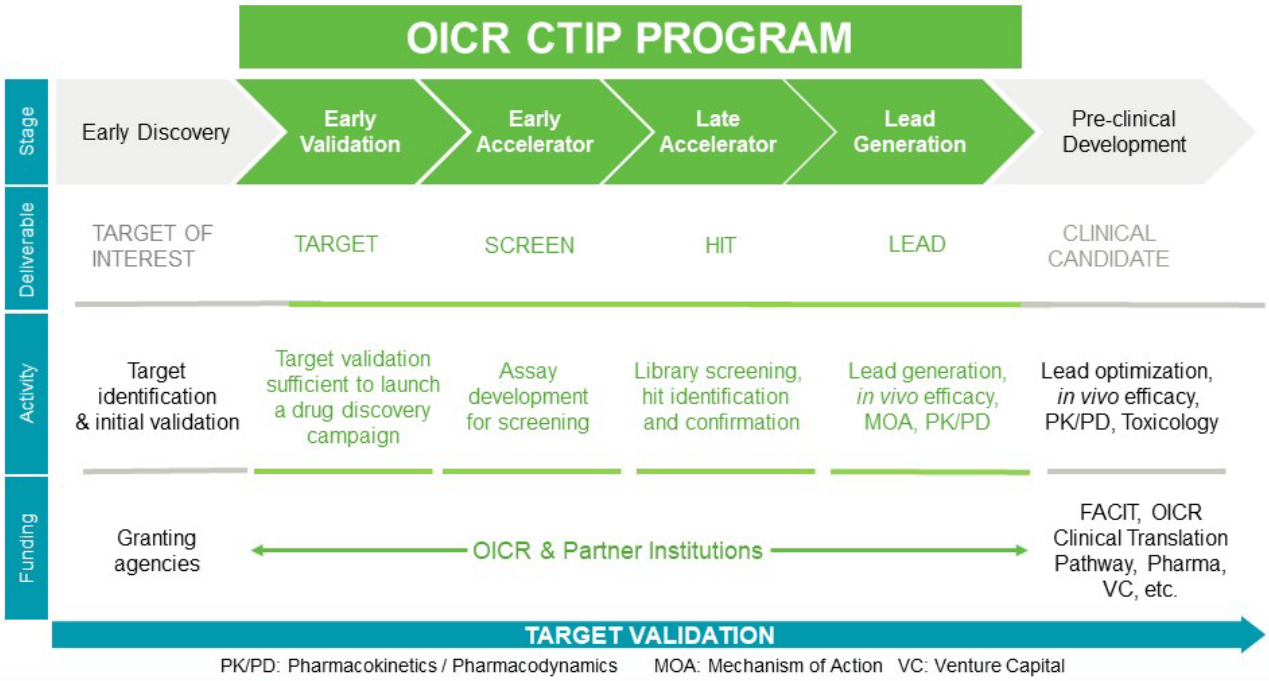


***Figure 1**: The Cancer Therapeutics Innovation Pipeline: Stages, deliverables, major activities, and funding sources.*

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. Expert and strict stage-gated strategic and scientific review is provided by the Therapeutics Pipeline Advisory Committee (TPAC), a group of highly qualified academic and industry experts with years of experience in drug discovery, systems biology and clinical trials.

1.3. CTIP projects

Understanding the relevance of a target in the pathophysiology of disease is repeatedly cited as the most critical factor in predicting the therapeutic value of modulating the activity of a putative target. During a drug discovery and development campaign, there is an absolute need to continually interrogate a target in the context of its biological function within a pathway(s) using functional assays, systems biology informatic tools and drug screening in increasingly complex *in vitro* and *in vivo* models that recapitulate the phenotype, genotype and systems of the cancer type of interest. **The generation of robust evidence of target validation and disease association, and a reasonably clear ultimate target clinical indication(s), are essential requirements of projects that enter and continue in the CTIP portfolio. Without sufficient evidence of target validation and disease association, projects will either not be accepted into the CTIP Program or will be terminated.** These parameters will be assessed together with feasibility, safety, and strategic considerations in the evaluation of a proposal's suitability for CTIP funding (see Appendix I). Applications will be discussed and assessed utilizing the criteria listed in the evaluation rubric.

With advances in science and technologies such as informatics, multi-omics (genome, epigenome, transcriptome, proteome, metabolome, microbiome, etc.), artificial intelligence, disease modelling and nanotechnologies, CTIP projects are expected to couple traditional target validation/disease association and screening approaches with state-of-the-art strategies such as querying of multi-omic and functional knowledge bases, selective perturbation of targets using

genomic tools, pharmacogenomic screening, patient-derived 3D or organoid modelling, biomarker identification and machine learning-inspired drug hunting, to name a few.

It therefore follows that the establishment of a drug discovery team should involve a collaboration of talent from different branches of science that includes, but is not limited to, biologists, chemists, biochemists, protein scientists, bioinformaticians, systems biologists, pharmacologists, biomarker experts, functional genomics experts, artificial intelligence scientists, imaging scientists, clinicians who regularly treat patients with the cancer of interest and data scientists. Furthermore, teams should endeavour to capture the voice of the cancer patient and their supporters in the design of their drug discovery campaign, as the experiences of patients and their families/friends bring much value to disease knowledge creation and to the conversation as to how their health should be managed.

Applicants are encouraged to reach out to the research community, preferably within the province of Ontario, as well as to the Drug Discovery Program at OICR and the Collaborative Research Resources (CRR) offered by OICR. CRR helps to enable research in Ontario by providing expertise, advice and access to research services on a cost-recovery basis. Researchers can benefit from OICR's high-end technology infrastructure, world-leading research knowledge, high-quality services and support. In addition, OICR funds major research initiatives in Adaptive Oncology and Clinical Translation and teams are encouraged to seek collaborations with investigators in these areas as they may be able to assist in buttressing the therapeutic target hypothesis and potentially contribute complementary expertise towards the achievement of CTIP deliverables, such as robust target validation.

In the event that a contract research organization (CRO) with the desired expertise, experience, model system(s) and track record of quality is available to conduct experiments efficiently and with rigour, or to generate high-quality reagents, the CTIP program will consider funding of such work. In this regard, OICR's Drug Discovery Program will work with the project team in the coordination and establishment of agreements with CROs.

Although this **RFA is limited to EV and EA applications only**, since successful projects have the potential to advance through the CTIP pipeline, the four stages of EV, EA, LA, and LG are described herein.

1.3.1. EV projects – Target-of-Interest to Target: Translational target validation and disease association

The goal of an EV project is to deliver robust translational evidence that a TOI is associated to a specific cancer type based on data from knowledge bases and from studies demonstrating that perturbation of the TOI in relevant cell-based or higher order models produces anti-cancer effects sufficient to trigger a drug discovery campaign.

Prerequisites: Entry into the EV stage requires demonstrable evidence of disease association to the cancer of interest, which **at a minimum** should include supportive data from:

1. Queries of multi-omics (genome, epigenome, transcriptome, proteome, metabolome, microbiome, etc.) and functional knowledge bases to ascertain the relevancy of the TOI in the cancer of interest as well as other cancer types.
2. Application of systems biology tools to:
   a) reveal redundancies and crosstalk within pathways, and identify associated pathway molecules that when perturbed, would be expected to result in phenocopying the effects of modulating the TOI.

b) identify potential correlative biomarkers and anti-targets.
c) expose any known potential off-target effects on molecules of similar molecular structure.

3. Perturbation (e.g., knockout/knockdown) of the TOI derived from the literature or generated in the applicants' laboratory which provides evidence for the relevance of the target in cancer. Building upon these preliminary results will form the core of the EV proposal in order to achieve the deliverables stated below.

Deliverables of an EV project: Demonstration that perturbation of the TOI in relevant cell-based models (including patient-derived lines whenever possible) or higher order systems using genomic (e.g., knockout/knockdown or upregulation/overexpression) and/or tool compounds supports target validation and disease association. At the end of the EV stage, there must be sufficient translational evidence to trigger a drug discovery campaign.

In addition, the team must describe the strategy they intend to take to prosecute the target during the EA stage. Preliminary evidence of the ability to interrogate the target with a sensitive, medium-to-high throughput primary screen must be presented by the end of the EV stage. Furthermore, the availability of relevant cellular models must be known prior to entry into the EA stage.

The project team should strive to replicate literature-sourced evidence within their own laboratories. Furthermore:

- Efforts must be made to demonstrate the effects in several cell lines which differentially express the target at the protein level and in a normal cell line control.
- The evidence must include results from control experiments using inactive or unrelated vectors.
- In knockdown or knockout experiments, rescue data supportive of target function is highly desirable.
- Pharmacologic or genetic manipulation of cell-based models used to mimic the conditions seen in human cancers (e.g., a specific protein or marker of stress) must be at levels that correlate with human data.

If feasible, development and validation of a tool compound to be used to interrogate the TOI can be included in the EV research plan. In addition, evidence from more complex 3D culture systems or existing animal models (from the applicant's own laboratory, another academic laboratory or a CRO) is desirable.

Team composition
Biologists and chemists with the expertise to generate robust evidence that supports the translation of a TOI into a relevant cancer drug Target must be on the EV project team. In addition, EV applicants must obtain input from a practicing clinician(s) in the relevant cancer type(s) to begin to define the target clinical indication(s) and the corresponding patient population. Furthermore, it is highly recommended that EV applicants identify a bioinformatics or systems biology collaborator or consultant to participate in the project.

Funding: EV projects will be funded up to $150,000 per year for a maximum of two (2) years.

1.3.2. EA projects – Target to Screen: Primary screen development

The goal of an EA project is to deliver a validated primary assay to enable initial screening of molecules against a defined target. Preliminary evidence of linearity of results between the primary assay and supporting secondary assays under development is also required.

Prerequisites: Entry into the EA stage requires translational target validation and disease association evidence as described in the EV stage above.

Deliverables of an EA project: A validated primary screening assay is the ultimate deliverable of an EA project. Performance of a small, focused screen using the primary assay to ascertain the feasibility of scale-up and preliminary evidence of linearity of results between the primary assay and supporting secondary assays under development are also required deliverables of the EA stage. At the end of the EA stage, teams must describe the strategy they intend to take to prosecute the target during the LA stage and demonstrate the capability and capacity to scale up production of reagents, recombinant proteins (as applicable), and relevant cell systems needed to support the medium-high throughput screening campaigns of the LA stage. The application of machine learning and artificial intelligence-inspired drug discovery and disease modelling would enhance the value of an EA proposal.

Funding: EA projects will be funded up to $150,000 for a maximum of one (1) year.

Team composition
Biologists and chemists with the expertise to generate robust evidence that supports the translation of a TOI into a relevant cancer drug Target must be on the EA project team. In addition, EA applicants must obtain input from a practicing clinician(s) in the relevant cancer type(s) to begin to define the target clinical indication(s) and the corresponding patient population. Furthermore, it is highly recommended that EA applicants identify a bioinformatics or systems biology collaborator or consultant to participate in the project.

1.3.3. LA projects – Screen to Hit: Hit generation

At this time, OICR is not inviting applications for LA projects.
The goal of an LA project is to deliver confirmed Hit molecules against a defined target using validated primary, secondary, and orthogonal assays for screening.

Prerequisites: Entry into the LA stage requires translational target validation and disease association evidence as described in the EV and EA stages above. The availability of a validated primary assay for screening of molecules against a defined target is mandatory, as well as performance of a small, focused screen using the primary assay to ascertain the feasibility of scale-up and corroborating preliminary results from supporting secondary assays. Demonstration of the capability and capacity to scale up production of reagents, recombinant proteins and/or cell systems needed to support the medium-high throughput screening campaigns of the LA stage is required. In addition, the LA application must describe the proposed mechanism of action that will be interrogated using appropriate LA stage assays.

Deliverables of an LA project: To deliver confirmed Hit molecules, the project must establish an integrated testing cascade consisting of primary, secondary, and orthogonal assays focused on demonstrating target binding, target engagement, target modulation (inhibition or activation), and pharmacodynamic and efficacy effects in cell-based models (including patient-derived lines whenever available) coupled with medium-to-high-throughput screening for Hits. LA projects should consider, when appropriate, the incorporation of more complex biological systems than cell lines (e.g., 3D cultures, spheroids, organoids) to further validate target-drug effectiveness and identify any off-target effects as well as potential toxicities. Depending on the target and the competitive landscape, initial *in vivo* data may be required by TPAC during the LA stage. At the end of the LA stage, the team must describe the strategy they intend to take to prosecute the target during the LG stage.

Funding: LA projects will be funded up to $500,000 per year for a maximum of two (2) years.

Team composition
Biologists and chemists with the expertise to generate robust evidence that supports the translation of a TOI into a relevant cancer drug Target must be on the LA project team. In addition, the LA project team must include a practicing clinician(s) in the relevant cancer type(s) to define the target clinical indication(s) and the corresponding patient population. Furthermore, LA applicants should have a bioinformatics or systems biology collaborator or consultant on the project team.

Eligible EV, EA and LA project activities:
EV, EA, and LA projects can include the following activities so long as they represent components of an integrated testing cascade that leads to a target with sufficient translational evidence of disease association (for an EV project), a validated primary assay to enable screening against a defined target (for an EA project) or confirmed Hit molecule(s) against a defined target (for an LA project):

- Functional genomic screens (e.g., knockdown or knockout experiments using RNA interference or CRISPR) and/or pharmacological knockdown using a tool compound
- Medium-to-high-throughput screens for large and/or small molecules
- Development and validation of biochemical and cell-based target engagement or modulation assays for screening and orthogonal target validation. Cell-based assays should clearly demonstrate whether perturbation of the target by leading molecules induces the death of cancer cells or only arrests cell proliferation
- Testing of patient-derived cell lines and 3D systems (spheroids or organoids)
- Structure-activity relationship (SAR) assessments to define minimum pharmacophores that demonstrate potential for further optimization
- X-ray structure generation
- Cross-target and cross-species selectivity assessments
- Characterization of *in vitro* pharmacokinetic properties (absorption, distribution, metabolism, excretion, ADME) and toxicology
- Computational approaches (e.g., virtual screening, machine learning, AI-inspired drug hunting and modelling)
- *In vivo* pharmacokinetics for representative molecules
- Assessment of the viability of candidate Hit molecules to support an LG effort
- Preliminary understanding regarding patient selection and how the medicine will be used in the clinic as a monotherapy or in combination in the course of the development and/or progression of the cancer indication.

1.3.4. LG projects – Hit to Lead: Lead molecules with demonstrated *in vivo* efficacy

At this time, OICR is not inviting applications for LG projects.
The goal of an LG project is to deliver high-quality Lead molecules (small and/or large), with demonstrated *in vivo* efficacy, ideally accompanied by pharmacodynamic and/or efficacy biomarkers, and markers of resistance (where applicable), that correlate with target modulation. Lead molecule profiles should be sufficiently mature to attract partnership/investment for further development and ultimately commercialization. To achieve this goal, the project must describe an integrated testing cascade of experiments which advances confirmed Hits into quality Lead series, coupling efficacy with target modulation. There must be an emphasis on establishing a connection between *in vitro, ex vivo,* and *in vivo* assays, and biomarker modulation (or other surrogate

measure of efficacy). Applications for the LG stage must fulfill the prerequisites for EV, EA, and LA projects as described above and must have confirmed Hit molecules to a defined target. In addition, LG proposals will require a preliminary biomarker plan and possible biomarkers for patient selection for drug therapy.

Prerequisites: Entry into the LG stage requires translational target validation and disease association evidence as described in the EV, EA, and LA stages above. The availability of confirmed Hit molecules against a defined target using validated primary, secondary, and orthogonal assays for screening is mandatory. In addition, the LG application must describe the proposed mechanism of action that was studied during the LA stage and articulate how that mechanism of action will be further interrogated in the LG research plan.

Deliverables of a LG project: To deliver high-quality Lead molecules, the project must establish an integrated testing cascade of experiments which advances confirmed Hits into quality Lead series, coupling efficacy with target modulation. It is critical that a connection between *in vitro* and *in vivo* assays, and biomarker modulation (pharmacodynamic and efficacy biomarkers, as well as markers of resistance as applicable), that translates to the human cancer of interest are demonstrated during this stage.

LG research plans must contain:

- A well-articulated hypothesis for modulation of the target as a treatment for the cancer type in the intended patient population.
- A preliminary biomarker plan and possible biomarkers for patient selection for drug therapy. Pharmacogenomic screening to identify and validate pharmacodynamic and efficacy biomarkers, as well as potential safety liabilities in response to drug treatment is required.
- A well-reasoned plan regarding patient selection and how the medicine will be used in the clinic as a monotherapy or in combination in the course of the development and/or progression of the cancer indication.
- A Target Product Profile (TPP) which summarizes the desired characteristics of the therapeutic asset, clinical development goals regarding safety and efficacy, and strategic elements that would confer a competitive advantage on the asset. The TPP should also include the patient's perspective on the attributes of the planned therapeutic. MaRS has developed some excellent resources to help develop a TPP scheme, which can be accessed here.

Funding: LG projects will be funded up to $1,000,000 per year for a maximum of two (2) years. It is recognized that some LG projects may require funding in excess of what OICR can provide to achieve the Lead molecule series deliverable. In such situations, applicants will need to identify leveraged funding or describe a plan to secure additional support from OICR or an external partner(s) during the funding period. Co-funding may be particularly important during the latter stages of an LG project when costs exceed OICR support, prompting the need to secure funds from other academic centres (e.g., host institution) or commercial partners, including FACIT, OICR's commercialization partner, based on commercial interest in the Lead molecule.

Team composition

Biologists and chemists with the expertise to generate robust evidence that supports the translation of a TOI into a relevant cancer drug Target must be on the LG project team. In addition, the LG project team must include a practicing clinician(s) in the relevant cancer type(s) to define the target clinical indication(s) and the corresponding patient population. Furthermore, LG

applicants must have a bioinformatics or systems biology collaborator or consultant on the project team.

Eligible LG project activities:

Projects entering the LG stage will possess Hit molecules characterized by a range of supporting evidence as described in the EV, EA, and LA stages. LG projects should include, but are not limited to, the following activities:

- SAR studies exhibiting a sufficiently broad dynamic range that would allow for optimization in potency, selectivity and safety, within chemical space where there is legal freedom to operate and the opportunity to generate intellectual property (IP)
- Experiments demonstrating differentiation in the context of the expected therapy in the target patient population (e.g., mechanism of action studies)
- Experiments that model how the medicine will be used in the clinic as a monotherapy or in combination in the course of the development and/or progression of the cancer indication
- Protein engineering studies (for large molecule therapeutics)
- Cell line generation and biophysical characterization for large molecule therapeutics
- Bioavailability studies using the intended route(s) of administration
- Pharmacodynamic (PD) and efficacy animal model development
- Dose ranging PD, PK and efficacy studies
- *In vivo* proof of concept or efficacy in a relevant biological system (animal model species) that will be used for margin of safety calculations
- Assessment of the viability of candidate Lead molecules to support a Lead Optimization effort

2. REQUEST FOR APPLICATIONS

This Request for Applications (RFA) is specific for investigators wishing to apply for funding support for an EV or EA project. **Submissions for LA and LG projects will not be considered under this RFA.**

2.1. Eligibility

OICR invites applications from investigators at Ontario academic centres, hospital research institutes or other government research institutions. **OICR funding is only tenable in Ontario. For profit entities are not eligible to receive OICR funding.**

Investigators are eligible to participate on and submit multiple CTIP submissions via this RFA.

Eligible projects must address the creation and protection of novel IP that will make drug candidates attractive to potential licensing and commercialization partners.

Drug re-purposing proposals will be considered by exception only. The proposal must possess a clear understanding of the mechanism of action and a plausible path to the development of a novel, method-of-use patent.

OICR is focused on developing and supporting the next generation of cancer researchers and strongly encourages applicants to include early career investigators/clinicians, particularly those from historically under-represented communities, as part of the study team. The inclusion of a patient or supporting individual(s) to the project team is also strongly encouraged especially for projects that are applying to enter the CTIP portfolio at the LG stage. Further, applicants should make note of the specific expertise requirements for the various CTIP stages (Section 1.3).

2.2. Term

The funding term start date for a funded CTIP application is December 1, 2024.

- The award term for **EV projects** is up to two (2) years (December 1, 2024 – November 30, 2026).
- The award term for **EA projects** is up to one (1) year (December 1, 2024 - November 30, 2025).

2.3. Funding available

- **EV projects** will be funded up to $150,000 per year, inclusive of overhead, for a maximum of two (2) years.
- **EA projects** will be funded up to $150,000, inclusive of overhead, for a maximum of one (1) year.

Annual funding is contingent upon available funding from the Government of Ontario via the Ministry of Colleges and Universities.

2.4. Eligible expenses

Expenses must adhere with OICR's guidelines for eligible expenses. The following expenses are not eligible under this RFA:

- Clinical/health intervention trials

2.5. Deadlines

CTIP applications are a three-step, competitive process, including a Notice of Intent (NOI), a Letter of Intent (LOI) and a full application.

ReportNet to open:	The week of April 8, 2024
Information session*:	April 24, 2024, 2-3 p.m. ET
NOI submission**:	No later than May 16, 2024 by 5 p.m. ET
LOI deadline:	May 16, 2024 by 5 p.m. ET
LOI results communicated:	The week of July 8, 2024
Full application deadline:	August 29, 2024 by 5 p.m. ET
Notification of results:	November 2024
Funding start date:	December 1, 2024

**Register here. This session will be recorded and posted on OICR's funding opportunities website.*
***The NOI form must be submitted prior to receiving access to the LOI and will be used for competition planning purposes. Information collected at the NOI stage **is editable** at the LOI stage.*

Late submissions will not be accepted.

For any questions, please refer to the FAQ page before contacting the OICR Scientific Secretariat office (ScientificSecretariat@oicr.on.ca).

2.6. Application requirements

IP, commercialization plan and recipient obligations

If invited to submit a full application, the research plan must include a brief, non-confidential description of any project-related IP and any restrictions or third-party rights impacting the IP development in Ontario. No commercialization plan is required for an EV, EA or LA application beyond a description of the use of proceeds for the proposed project. It is strongly suggested that

this IP and commercialization section of the RFA be reviewed together with institutional Technology Transfer Officers.

Since the ultimate goal of this program is to support translation of new cancer therapies to the clinical setting, the creation and protection of IP that will make drug candidates attractive to potential licensing and commercialization partners is a significant consideration in prioritizing projects for funding. CTIP is structured so that the awardee Host Institution(s) retains background IP rights. In line with the provincial government's "Ontario First" mandate, which requires that reasonable efforts are undertaken to commercialize and manufacture a project's arising IP in Ontario, applicants will contractually agree to oversight by FACIT, OICR's commercialization partner, to finalize the commercialization planning, rights and obligations, with an emphasis on Ontario-based development.

Award agreements will include an Option for FACIT to act as the commercial agent for any arising IP. In order to balance academic commercialization freedom and to be in line with other similar programs, the Option will be restricted to the period during the EV, EA or LA project and a three-month period following the completion of the project. Further, should an LA project evolve into a LG project, OICR funding of EV, EA and LA research activities will be added to any investments made by OICR during the LG stage in the determination of OICR's total contributions to the project.

Patient partners

Patient perspectives and insight can be transformative to research planning, execution and knowledge transfer. Patient partnership in OICR-supported research ensures i) studies meet the needs of the people intended to benefit, and ii) study activities and results are communicated in an accessible way to patients, caregivers and the wider community. All full applications must include a patient partnership plan, in which applicants describe how patient partners and stakeholder communities are being, or will be, engaged throughout the life cycle of the project. Applicants are encouraged to involve patient partners as early as possible in the application process, as they can help shape the research question, develop the patient partnership plan, and inform the writing of the lay summary. Teams can explore the resources available on the Patient Partnership page of the OICR website and at their home institutions on how to recruit and involve patient partners and communities into the research process. Members of OICR's Patient and Family Advisory Council (PFAC), or delegates, will participate in the full application review, as well as progress reviews to provide ongoing guidance over the funding term.

Equity, Diversity and Inclusion

All OICR-supported research is expected to align with the Institute's principles of Equity, Diversity, and Inclusion (EDI). OICR's Commitment to EDI in Research Statement can be found on our website. OICR is committed to:

- Ensuring our research serves those from all relevant communities, especially those that are historically underrepresented
- Fostering a more diverse and inclusive research community
- Creating a work environment where all can thrive and feel included
- Collecting and analyzing demographic data to better understand the diversity of applicants, funded researchers and project teams in order to identify gaps and develop approaches to address those gaps
- Continuing to evaluate our processes, ask for input, collect data and improve
- Communicating how we will achieve equity, diversity and inclusion

- Sharing best practices and lessons learned to help drive equity, diversity and inclusion across the cancer research community

Refer to OICR's guidelines on Equity, Diversity and Inclusion tactics in research for more details.

Declaration of Research Assessment
OICR is a signatory to the San Francisco Declaration of Research Assessment (DORA). As such, we are aligned with DORA principles through our commitment to assess the quality and impact of scientific research through means other than journal impact factors. As part of OICR's commitment to these principles, applicants are asked NOT to include journal impact factors (JIF) or other journal-based metrics in any document submitted as part of the application process.

Use of Artificial Intelligence
OICR aligns with the recent statement from CIHR on the use of artificial intelligence (AI) to write grant applications. As with CIHR, OICR expects that applicants will draft proposals and supporting text themselves; use of AI to draft application materials will be considered plagiarism as per the Tri-Agency Framework: Responsible Conduct of Research.

Reviewers must also abstain from the use of AI when drafting their feedback and must never copy/paste applications (or excerpts) into AI platforms as doing so will constitute a breach in confidentiality.

2.7. Overview of application requirements using the online submission system

CTIP applications are a three-step process including a Notice of Intent (NOI), Letter of Intent (LOI) and a full application. All three stages are to be submitted using ReportNet, OICR's online system for managing grants and awards. Refer to OICR's guidelines on using ReportNet for additional information.

Uploaded files must be in 11-point Arial font with single spacing and one-inch margins.

2.7.1. Accessibility and Accommodations

Providing an accessible experience is important to us. If you require an accommodation in order to prepare or submit an application, or if you require documents or materials in an alternative format, please contact the Scientific Secretariat (ScientificSecretariat@oicr.on.ca) to discuss opportunities. More information on OICR's Accessibility Plan can be found on our website.

2.7.2. Completing a Notice of Intent

The NOI collects basic application information and will be used by OICR for planning purposes. **An NOI must be submitted prior to gaining access to the LOI form**. The information provided in the NOI can be updated prior to submitting the LOI. The deadline for submission of the NOI is the same as the deadline for LOI submission, however, applicants are encouraged to submit their NOI as early as possible to assist with planning and to ensure sufficient time to complete the LOI by the deadline.

Application information

The system will pre-populate the PI's information from their ReportNet profile. Applicants will not be able to submit without first completing their user profile, including the demographic questions.

Additional information, some of which is outlined below, is to be provided by the applicant(s). Required fields are marked with a red asterisk in ReportNet. Word/page counts, where applicable, are noted. Investigators and other collaborators can be added to the submission using the 'Invitations' tab on the left side of the screen.

- **What project category are you applying for?** Only EV or EA projects are eligible under this RFA; select the appropriate category for your proposal.
- **Title**
- **Start date:** Enter a funding start date for the application, no earlier than December 1, 2024.
- **End date:** Enter a funding end date for the application. EV projects can be a maximum of two (2) years; EA projects can be a maximum of one (1) year.
- **Key words**
- **Cancer type**

Once you have completed all required fields, select the green '*Submit and Continue to LOI*' button at the bottom of the screen. You will immediately be provided with access to the LOI form.

2.7.3. Completing a Letter of Intent

Information provided in the NOI will be carried over to the LOI form and is editable.

- **Application type:** Indicate whether this proposal is a resubmission of a previous CTIP application. If 'Yes' is selected, additional information will be requested, including a requirement to upload the Scientific Officer and reviewer reports from the initial application, and a response to previous feedback (max. 500 words).
- **Has this work been published/patented?** (max. 200 words)
- **Target and/or pathway** (max. 25 words)
- **Molecule type**
- **Target class** (max. 25 words)
- **Lay summary** (max. 500 words): The lay summary should explain complex research ideas in simple terms and plain language that can be easily understood by non-scientists at the high school graduate level. This is unlike a scientific abstract, which is written for subject peers. The lay summary will be used by reviewers and patient partners during the review process. If funded, it may be used to communicate your research to the public and funders. The applicants are strongly advised to engage a patient partner to co-write or review the lay summary.

  An overview of each of the following topics is recommended, as applicable:
  - Background/context to the research
  - Description of the current standard of care
  - Research question and the specific clinical problem to be addressed
  - Thorough description of proposed research/method(s)
  - Potential benefit to patients/impact on the field.

  Bullet points are acceptable to highlight key points. Please use plain English while avoiding acronyms, scientific jargon and technical, field-specific terms unless a short explanation is added. Short sentences with easy sentence constructions are advisable.

  The lay summary may be shared with external parties for communications and reporting purposes, and with reviewers to identify potential conflicts of interest. **In addition, the project title and lay summary should refrain from identifying the target because the CTIP**

Program has a goal of developing novel IP. Both the project title and the lay summary should be considered non-confidential.

- **Scientific summary** (max. 500 words)
- **Proposed budget** (max. 250 words): describe the high-level budgetary requirements and any current funding allocated to the project.
- **Research plan – LOI**
  Address the items below in the provided textboxes. **Bulleted lists are strongly encouraged where appropriate**:
  - **Aims** (max. 250 words)
    - Provide specific aims that will address key issues for the project.
  - **Target validation and disease association** (max. 750 words)
    - Define the project hypothesis and the specific clinical problem to be addressed, specifying the desired mechanism of modulation (e.g., inhibitor, agonist, etc.) and the intended modality (e.g., small molecule, biologic, etc.).
    - Provide bioinformatics and systems biology queries of relevant knowledge bases (e.g., DepMap, TCGA, cBioPortal, MalaCards, etc.) showing clear disease indication association and/or target dependency of the disease area.
    - Describe the target's function and interactions with other players in the pathway(s).
    - Provide the scientific and clinical evidence supporting prosecution of the target for the treatment of the cancer type in the intended patient population. This must contain the minimal requirements for portfolio entry as described in section 1.3.
    - Describe gaps or uncertainties related to target validation and disease association, and research plans to address these.
  - **Safety** (max. 250 words)
    - Describe any known or potential toxicology considerations and plans to monitor these liabilities.
    - Provide data on published knockout models indicating safety and little or no off-target effects.
    - Describe any known or suspected toxicity with other previously developed drugs hitting the same pathway of the proposed target.
  - **Feasibility** (max. 500 words)
    - Describe the primary screening assay(s) that the team plans to validate (for EA proposal) or has validated (for LA proposal) and the status and performance of the assay(s).
    - For a LA proposal, provide information on the capability and the resources available to the applicant to support target enablement and primary screen development (e.g., scale up of reagents, recombinant proteins, cell lines including patient-derived lines, controls, etc.)
    - Describe all secondary and orthogonal assays (e.g., target engagement, selectivity, cell-based, etc.) to be used for confirming Hit molecules (LA stage deliverable) and the status and performance of the assays.
    - Provide information on the resources available to the applicant to support development of all secondary and orthogonal assays.
    - Describe the chemical collections to be used for primary screening.
    - Describe the Hit (for LA proposal) or Lead (for LG proposal) generation strategy and the tools needed to execute on that strategy (e.g., crystal structure or homology models, medicinal chemistry or biologics-based approaches).
    - Specify the biomarkers (pharmacodynamic, efficacy and/or resistance) to be measured and if they have been validated or a plan to address validation.

- Describe the team composition and collaborations, planned or in place, and the expertise that will be contributed to the project by each PI and collaborator.
- Separately upload a testing cascade. The testing cascade must not exceed one page. Refer to Appendix II for an example.

- **Strategic considerations** (max. 500 words)
  - Describe the unmet clinical need, identifying the current standard of care for the disease indication, and its limitations.
  - Describe the competitive landscape and the differentiation features of the proposed therapeutic approach.
  - Describe issues with contemporary efforts with the same or related target including reasons for successes or failures based on biologic, pharmacologic or toxicity concerns.
  - Indicate if molecules identified from this effort have the potential to be FiC or BiC potential.

- **Attachments**: The following items should be attached to the LOI:
  - **Figures and tables** (max. of six figures and tables). Each figure should be uploaded separately as a single page jpeg file. Label file name: Request ID_Figures tables #X_LOI. A legend can be provided for each figure/table in the provided textbox.
  - **Testing cascade – LOI** (must not exceed one page; refer to Appendix II. Label file name: Request ID_ Testing cascade_LOI and upload as a jpeg).
  - **References.** Label file name: Request ID_References_LOI and upload as a PDF.

Once you have completed all required fields, select the green '*Submit LOI*' button at the bottom of the screen.

2.7.4. Completing a full application

Information provided at the NOI and LOI stage will be carried over to the full application form and, with the exception of items under the '*LOI Research Proposal*' and '*LOI Attachments*' sections, will be editable. Only applicants invited to submit a full application following the LOI review will be provided with access to the full application form.

The following information will be required for a full application:

- Research ethics attestation
- Equity, Diversity and Inclusion considerations and plan
- Regulatory Requirements
- Common Scientific Outline
- Administrative authority contact information

Application checklist

Applicants must confirm that their proposal meets the criteria of the CTIP funding stream to which they are applying. If a proposal does not meet the criteria, the project may not be suited for CTIP funding at this time.

Research proposal

Research plan – Upload (max. 10 pages. Label file name: Request ID_Research Plan_Full and upload as a PDF): Using the headings indicated, provide details on the proposed research. The research plan must **expand** upon the content provided at the LOI stage (black bullets below) as well as address the additional full application requirements (blue bullets below).

- **Aims**

- Provide specific aims that will address key issues for the project. Each aim must match to a deliverable(s) and associated milestones (deliverables and associated milestones are described below).

- **Target validation and disease association**
  - Define the project hypothesis and the specific clinical problem specifying the desired mechanism of modulation (e.g., inhibitor, agonist, etc.) and the intended modality (e.g., small molecule, biologic, etc.).
  - Provide bioinformatics and systems biology queries of relevant knowledge bases (e.g., DepMap, TCGA, cBioPortal, MalaCards, etc.) showing clear disease indication association and/or target dependency of the disease area.
  - Describe the target's function and interactions with other players in the pathway(s).
  - Provide the scientific and clinical evidence supporting prosecution of the target for the treatment of the cancer type in the intended patient population. This must contain the minimal requirements for portfolio entry as described in section 1.3.
  - Describe gaps or uncertainties related to target validation and disease association, and research plans to address these.
  - Describe the intended route of administration.
  - Describe the mechanism of action and related pathway pharmacology.
  - Describe how the drug will be used in the clinic as monotherapy or in combination therapy.
  - Describe how patients would be selected for the proposed therapeutic.
- **Safety**
  - Describe any known or potential toxicology considerations and plans to monitor these liabilities.
  - Provide data on published knockout models indicating safety and little or no off-target effects.
  - Describe any known or suspected toxicity with other previously developed drugs hitting the same pathway of the proposed target.
- **Feasibility**
  - Describe the primary screening assay(s) that the team plans to validate (for EA proposal) or has validated (for LA proposal) and the status and performance of the assay(s).
  - For an LA proposal, provide information on the capability and the resources available to the applicant to support target enablement and primary screen development (e.g., scale up of reagents, recombinant proteins, cell lines including patient-derived lines, controls, etc.).
  - Describe all secondary and orthogonal assays (e.g., target engagement, selectivity, cell-based, etc.) to be used for confirming Hit molecules (LA stage deliverable) and the status and performance of the assays.
  - Provide information on the resources available to the applicant to support development of all secondary and orthogonal assays.
  - Describe the chemical collections to be used for primary screening.
  - Describe the Hit (for LA proposal) or Lead (for LG proposal) generation strategy and the tools needed to execute on that strategy (e.g., crystal structure or homology models, medicinal chemistry approaches).
  - Specify the biomarkers (pharmacodynamic, efficacy and/or resistance) to be measured and if they have been validated or a plan to address validation.
  - Separately upload a testing cascade. The testing cascade must not exceed one page. Refer to Appendix II for an example.
  - Describe plans to address issues associated with primary, secondary and orthogonal assay development including the acquisition of key assay components and reagents.

- Specify any interactions with OICR's Drug Discovery Program, Collaborative Research Resources or other research areas under OICR's Adaptive Oncology and Clinical Translation themes.
- Describe the desired selectivity profile, including any intentional polypharmacology.
- Summarize host/partner institution facilities and resources available to support research execution.

- **Strategic considerations**
  - Describe the unmet clinical need, identifying the current standard of care for the disease indication, and its limitations.
  - Describe the competitive landscape and the differentiation features of the proposed therapeutic approach.
  - Describe issues with contemporary efforts with the same or related target including reasons for successes or failures based on biologic, pharmacologic or toxicity concerns.
  - Indicate if molecules identified from this effort have the potential to be FiC or BiC potential.
  - The research plan must include a brief non-confidential description of any project-related IP, and any restrictions or third-party rights impacting the IP development in Ontario (see section 2.6).
  - Describe patient selection opportunities.
  - Provide an estimate of the size of the target patient population.
  - Describe any known or anticipated hurdles associated with regulatory approval, adoption of the therapeutic by patients or clinicians, and reimbursement of the medicine.

Additional information

- **Patient and/or partner engagement** (max. 250 words): Patient perspectives and insight can be transformative to research planning and execution. Applicants should address how patient partners and communities are being, or could be, partnered with throughout the life cycle of the project. This section must be written as a stand-alone piece, assuming that readers may not have read the application research proposal. It should be written in clear, easy to understand, lay language understandable to a high school graduate.
- **Differentiation** (max. 250 words): Provide a description on what makes this research unique, better and/or disruptive compared to what other researchers are working on in your field (i.e., what is distinguishing about this research that makes it more attractive than other existing work). This information may be shared with FACIT, OICR's commercialization partner, should the proposal be funded.
- **Data management plan** (max. 500 words): Applicants must provide a data sharing and access plan, as well as a data storage requirements and retention plan, specifying how much data will be generated or transferred into OICR (if applicable) during the course of the project, and the plan for retaining/archiving with the ability to restore the data for the five-year period following its conclusion. Refer to OICR's guidelines on data retention, sharing and open access for more information.
- **Team composition**: Using the template provided, describe the members of the team (if there is more than one person working on a particular deliverable, indicate the number of persons assigned), their expertise, what activity they will be conducting in accordance with the testing cascade, and which deliverable(s) and associated milestone(s) they will be responsible for. Label file name: Request ID_Team composition_Full, and upload as a PDF.

Attachments

The following items should be attached to the application:

- Figures, tables and references (max. of 12 figures and tables). Label file name: Request ID_Figures tables ref_Full, and upload as a PDF.
- Testing cascade – Full application (must not exceed one page; refer to Appendix II. Label file name: Request ID_Testing Cascade_Full, and upload as a PDF).
- Host institution attestation: Using the PDF form provided, the applicant must obtain the signature of the institutional administrative authority attesting to the terms outlined in the form. Additional forms should also be signed and uploaded from the Host Institution of any Co-PIs. Label file name: Request ID_HI attestation, and upload as a signed PDF. If the host institution for a PI or Co-PI is OICR, an attestation form from OICR is not required.
- Deliverables and milestones, using the Excel template provided (Label file name: Request ID_DM, and upload as an Excel file)
    - Deliverables are pre-defined outputs or outcomes that describe what success looks like for the project. When achieved, deliverables must provide meaningful impact towards achieving the goal of the proposal. Milestones are points in the research plan that facilitate measurement of progress towards the achievement of the deliverable. These deliverables and milestones will be used to measure research progress during progress updates.
    - Specify high-level deliverables that are projected to be achieved during the funding term.
    - For each deliverable, specify at least two associated milestones. Milestones will be monitored to assess progress towards achievement of the deliverable. **Milestones that specify go/no go decision points must be included. A go/no go decision point dictates that achievement of the milestone is essential to move to the next set of dependent activities.**
    - Both deliverables and milestones must be measurable and possess a target date for completion (provide the quarter and fiscal year of projected achievement).
- Budget, using the Excel template provided (Label file name: Request ID_Budget, and upload as an Excel file)
    - Download the budget template provided in the application and complete budget request details. Expenses must adhere with OICR's guidelines for eligible expenses. The following expenses are not eligible under this RFA:
        - Clinical/health intervention trials
    - The template will automatically calculate overhead at thirty per cent (30%) for overhead eligible expenses for non-MaRS based institutions. The overhead rate can be adjusted on the 'info and instructions' tab. Please contact the Scientific Secretariat with any questions regarding overhead. **Overhead must be accounted for in the budget requested which cannot exceed the maximum amounts stated in section 2.3.**
- CVs
    - Compile CVs (**abbreviated CVs are encouraged**) for the following individuals (label file name: Request ID_CVs, and upload as a single, bookmarked PDF):
        - PIs and Co-PIs
        - Co-Investigators
    - CVs can be in any format so long as it addresses:
        - Education/training
        - Employment
        - Honours and awards
        - Professional affiliations
        - Research funding in the past five years
        - Research outputs (e.g., publications, IP, presentations, etc.)
- Other
    - Include a list of all current and pending funding applications, highlighting any overlap with the present application (label file name: Request ID_Funding apps, and upload as a PDF.

- Co-funding letters, if applicable (label file name: Request ID_Co-funding letter, and upload as a single, bookmarked PDF): Provide evidence of co-funding through a letter of support from the funder. Include whether funds are cash vs. in-kind, and whether they are secured vs. expected. Co-funding should also be captured in the Excel budget template. Provide evidence of co-funding through a letter of support from the funder. Include whether funds are cash vs. in-kind, and whether they are secured vs. expected. Co-funding should also be captured in the Excel budget template.

Once you have completed all required fields, select the green '*Submit*' button at the bottom of the screen.

3. REVIEW PROCESS

3.1. LOI review

LOIs will be reviewed by TPAC, and *ad hoc* experts, if required, along the four themes of target validation/disease association, safety, feasibility and strategic considerations (Appendix I).

Reviewers will provide feedback and an overall recommendation ('Yes to full application', 'No to full application', or 'Requires discussion').

LOIs that receive a 'No' recommendation from all assigned reviewers may be triaged prior to the panel discussion. Only LOIs that are ranked 'Yes' by all assigned reviewers after the panel discussion will be invited to submit a full application.

If the number and quality of LOIs received far surpasses the number of applications that can reasonably be reviewed at the full application stage, TPAC will be asked to score proposals in order to establish a cut-off that will be used to triage applications.

3.2. Full application review

Administrative review

An administrative review may be completed by the OICR Scientific Secretariat in order to assess the submission for conformity with the guidelines. Relevant points from the administrative review will be shared with the PI.

External peer review

Review panel

Full applications will be reviewed by a panel consisting of TPAC and *ad hoc* experts, if required. The panel's mandate will be to evaluate the merits of the applications. Panel members will be assigned to applications as primary, secondary, and tertiary reviewers and will provide a brief preliminary report outlining their feedback on the proposal.

Patient and Family Advisory Council (PFAC)

Applications may be shared with the OICR PFAC, or their delegates, who will review applications and may provide written feedback to the review panel in advance of the full application review meeting. As deemed appropriate by the review panel, PFAC feedback may be provided to applicants as part of the SO report that will be provided to teams following the review meeting.

Reviewer reports

Reviewers will be tasked with providing a brief report for their assigned projects using the following criteria (see Appendix I for additional information):

- Target validation/disease association
- Safety
- Feasibility
- Strategic considerations

Reviewers will also provide an overall score for the application as a whole. The overall score may be used for ranking applications, if deemed appropriate by the review panel Chair. Reviewers will also be asked to indicate whether the proposal should be in contention for funding and evaluated further at the full application review meeting (Yes, No or Undecided). Applications that receive a 'No' from each of the assigned reviewers may not be discussed further at the review meeting.

Review meeting
Depending on application pressure, and with the approval of the TPAC Chair, applications may be ranked by overall score prior to the review meeting so that only the top applications in contention for funding are discussed. The panel will have an opportunity to review the rankings in advance of the meeting, and, if appropriate, revise the order.

The meeting will be moderated by the TPAC Chair with support from OICR's Scientific Secretariat and will include representatives from OICR and PFAC (if appropriate). Following open discussion, the panel will recommend a consensus overall score by which the application will be ranked. Highly ranked applications, which are deemed meritorious for funding, will be recommended for approval to OICR leadership.

3.3. Notification of Decision

A meeting report summarizing the review discussion and recommendation for each application will be prepared by a Scientific Officer and distributed to applicants, along with anonymized reviewer reports, as part of the Notification of Decision (NOD) from OICR.

OICR intends to provide NOD letters to all applicants in November 2024. Funding will start on December 1, 2024 for successful applicants. Applications recommended for funding will receive a Notice of Award outlining next steps in order to accept the award and establish a funding agreement.

4. ESTABLISHMENT OF AGREEMENTS

Following approval of the proposal, OICR will establish a funding agreement with the Host Institution of the Lead PI and Partner Institutions (if applicable). The agreement will cover the general principles regarding the conduct of research activities, eligible research expenses, terms and conditions regarding the disbursement of funds, agreements with third-party funders, financial and progress reporting, PI/Co-PI covenants, IP, commercialization, publications and communication policies. In addition, OICR will establish a commercialization framework, which will require the recipient and OICR to set up an IP co-management plan, where applicable.

Note that delays in execution of research agreements may impact OICR's ability to disburse funds. **Funding is contingent upon available funding from the Government of Ontario via the Ministry of Colleges and Universities.**

5. REPORTING REQUIREMENTS

Financial and operational status reporting

The following schedule (Table 1) will be used for financial and operational status reporting. Note that the deadlines indicated are moved to the next business day if they fall on a non-working day. A quarterly reporting template and instructions will be available on the OICR online financial reporting system, CaAwardNet.

Financial Officers of the Lead Institution will be required to provide quarterly updates on budget versus actual expenditures as per the table below. When reporting on the operational status of a project, an explanation of variances of greater than ±15 per cent and mitigation plans to address the budget gaps should be provided.

***Table 1**: Financial and operational status reporting*

Period covered	Responsible party and action	
	Financial Officer	**PI at Lead Institution (or designate)**
Q1 April-June	Quarterly financial report Due: July 31	Review and submit quarterly financial and operational status report Due: August 15
Q2 July-September	Quarterly financial report Due: October 31	Review and submit quarterly financial and operational status report Due: November 15
Q3 October-December	Quarterly financial report Due: January 31	Review and submit quarterly financial operational status report Due: February 15
Q4 January-March	Quarterly financial report Due: April 30	Review and submit financial and operational status report Due: May 15
Q1-Q4 April-March	Annual fiscal year financial report: Due May 31	N/A

Progress and Key Performance Indicator (KPI) Reporting

All projects will be included in OICR's annual reporting process, as required by the Ministry of Colleges and Universities according to the schedule below (Table 2). Note that the deadlines indicated are moved to the next business day if they fall on a non-working day.

***Table 2**: Reporting requirements*

Report	Period covered	Due date	Person(s) responsible	Action
Progress update	Q1-Q2	Q3	PIs/Co-PIs	Provide status updates on Deliverables and Milestones (D/M), progress update to TPAC

Progress update	Q3-Q4	Q1	PIs/Co-PIs	Provide status updates on D/Ms, progress update to TPAC
KPI report	Fiscal year: April-March	April 30 of the subsequent fiscal year	PIs/Co-PIs	Provide quantitative KPIs using ReportNet (OICR's online submission system)

6. COMMUNICATION WITH OICR

The obligations of the investigators to advise OICR of anticipated public dissemination, publications and media announcements will be outlined in the research agreement.

7. ACKNOWLEDGEMENT AND RECOGNITION OF SUPPORT

All investigators and recipient institutions must acknowledge and credit the contribution/support, in whole or part, of OICR and the Government of Ontario in any promotional material, including, without limitation, scientific publications of whatever nature or kind, and in any communication materials or publications supported by OICR funding by referencing the projects/subprojects with the following statement: "This study was conducted with the support of the Ontario Institute for Cancer Research through funding provided by the Government of Ontario. The views expressed in the publication are the views of the authors and do not necessarily reflect those of the Government of Ontario".

8. CONTACT INFORMATION

For any questions, please refer to the FAQ page before contacting the OICR Scientific Secretariat office (ScientificSecretariat@oicr.on.ca).

9. APPENDIX I: EVALUATION RUBRIC AND SCORING CRITERIA

OICR is a signatory to the San Francisco Declaration of Research Assessment (DORA). Reviewers at all stages of the OICR grant application process are advised that they should consider the quality of the research published and/or proposed in an application. While productivity may be an important factor, the assessment will be based on the content of articles and not the JIF. Furthermore, OICR reviewers are asked to consider the influence of candidates' publications in advancing knowledge in a given field (or throughout biology).

LOIs and full applications will be assessed by the Therapeutics Pipeline Advisory Committee (TPAC) using an evaluation rubric developed along four themes of inquiry:

- Target validation/disease association
- Safety
- Feasibility
- Strategic considerations

The rubric below is meant to provide *guidance* for discussion and feedback to the teams. If additional guidance is required, reviewers should reach out to the Scientific Secretariat for assistance. The application will be discussed and evaluated against the listed criteria, where applicable.

Table 3: *Evaluation rubric for CTIP proposals*

Target validation/disease association	Safety	Feasibility	Strategic considerations
Human disease altered by drugs hitting target and/or target pathway from Phase II, III or post-marketing decision clinical trial data	Toxicity liabilities can be tracked and are manageable	Relevant *in vivo* models with and efficacy endpoints	Clinical need
Promising Phase I-IIa clinical trial data with other drugs hitting the target and/or target pathway or similar biology	Toxicity profile of known ligands understood	Relevant *in vivo* models with pharmacodynamic endpoints	Clinical delivery
Biomarker for target dependence understood in the disease	Toxicity liabilities in genetically modified animals is understood	Relevant organoid-based assays with relevant endpoints	Target patient population
Preclinical, dose-dependent efficacy modeling predictive of human efficacy, with human genetic evidence	Toxicity liabilities of the pathway, anti-targets and isoforms understood	Relevant patient-derived cell-based assays with relevant endpoints	Market opportunity
Intervention at target in pathway using selective tool compounds demonstrates preclinical efficacy	Toxicity assays are available and affordable for the stage	Relevant cell-based assays (immortalized cell lines) with relevant endpoints	Differentiation: First-in-class or Best-in-class potential
Transgenic or knockout animals have disease phenotype	Toxicity liabilities can be measured	Biomarker(s) identified and validated	Competitive landscape and

Target validation/disease association	Safety	Feasibility	Strategic considerations
	reproducibly		history of successful or unsuccessful targeting of the major pathway or organelle under question
Data implicating target in disease state pathogenesis and/or demonstrated pharmacology in pathway		Selectivity assays (target class and target-specific isoforms) with no undue risk that required recombinant proteins or protein complex cannot be synthesized	Freedom to operate
Pharmaceutical intervention at the target unproven but suggestive research		Availability of computational expertise	Regulatory considerations
Transgenic or knockout (including shRNA or CRISPR *in vivo* models) animals demonstrate linkage to physiology and/or disease		Availability of crystal structure or homology model	Reimbursement
Loss or gain of function in patient-derived organoids shows disease phenotype		Feasibility of structure-based drug design	
Loss or gain of function in patient-derived cell-based assay shows disease phenotype		Confirmatory/binding assays	
Target function linked to pathway which is abnormal in the disease based on cell biology research		Biochemical inhibition assays	
Loss (e.g., shRNA, CRISPR, partially selective tool compounds) or gain (e.g., overexpression) of function phenotype in immortalized cell lines		Feasibility of protein complex assembly suitable for screening	
Target function linked to disease progression and/or poor prognosis		Availability/feasibility of key screening reagents (e.g., target, recombinant proteins, functional domains, inactive constructs, selectivity reagents, etc.)	
Target tissue distribution known		Availability of chemical collections for screening	

Target validation/disease association	Safety	Feasibility	Strategic considerations
New therapeutic hypothesis or disease association of target by clinical genetics (e.g., mutation, amplification, translocation)		Team composition and collaborations	
Disease hypothesis based on pathway or related protein biology			

Full applications for CTIP projects will receive scores for each theme outlined in the evaluation rubric above (Table 3), as well as an overall score for the project. The final overall score will be used to rank projects for funding consideration. Scores will be assigned as outlined in Table 4.

Table 4: *Scoring*

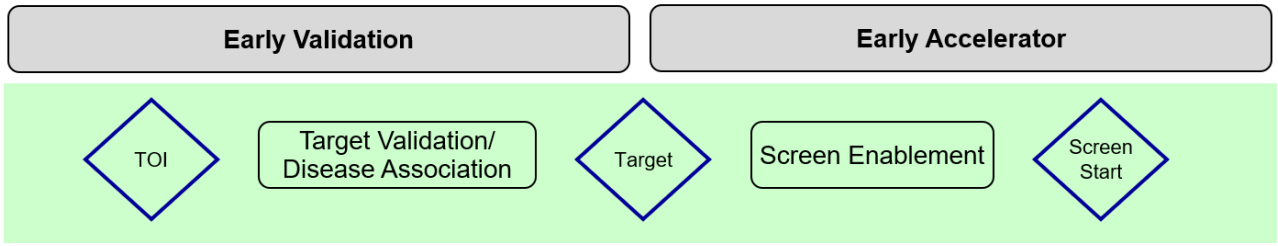
Overall impact	Score	Description
High	8	Excellent with no weaknesses identified
	7	Excellent with minor weaknesses identified
Medium	6	Very good with minor weaknesses identified
	5	Very good with moderate weaknesses identified
	4	Good with moderate weaknesses identified
Low	3	Fair with moderate weaknesses identified
	2	Poor with moderate to major weaknesses identified
	1	Poor with major weaknesses identified

10. APPENDIX II: TESTING CASCADE

The images in Appendix II (Figures 2, 3 and 4) are the property of the Ontario Institute for Cancer Research.

***Figure 2:** Testing cascade for Early Validation and Early Accelerator projects*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes).
- Critical path assays should be in solid boxes, profiling assays in dotted boxes.
- Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.



- Disease association
- Biochemical pharmacology or cell/molecular biology research linking target function to a physiological pathway which is abnormal in disease
- Functional genomic screens (e.g., shRNA, CRISPR)
- See section 1.3 of the Request for Applications for additional details

- Material Prep (e.g., protein, antibodies, cells)
- Primary screening assay development & validation
- Secondary assay development & validation

Criteria:
Validated primary assay against a defined target

KEY
Green: Assay Validated (pharmacology + stats)
Yellow: Assay in development
Red: Assay Not Ready
Critical path assay
Profiling assay

Figure 3: *Testing cascade for Late Accelerator projects (**note: Late Accelerator projects are not eligible for this RFA but provided for information**).*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes).
- Critical path assays should be in solid boxes, profiling assays in dotted boxes.

Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.

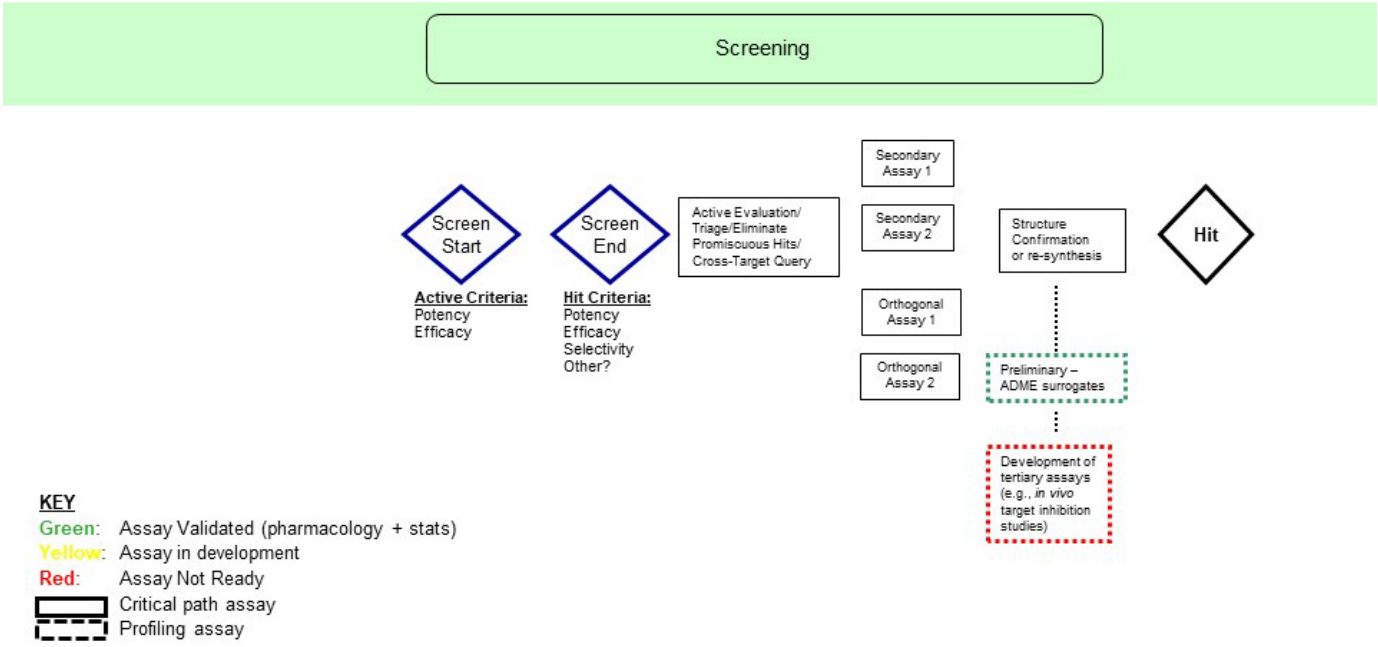


Figure 4: *Testing cascade for Lead Generation projects (**note: Lead Generation projects are not eligible for this RFA but provided for information**).*

- The testing cascade should identify which assays are completely validated (in green boxes), in progress (yellow boxes), or required (red boxes).
- Critical path assays should be in solid boxes, profiling assays in dotted boxes. Statistical validation data (both inter- and intra-assay) should be listed and documented in a supporting document.