September 20, 2025

Geoffrey Ogram Memorial Research Grant Reviewing Panel
c/o Lung Cancer Canada

Re: Letter of Intent – Pre-PLaN Study

Dear Members of the Reviewing Panel,

I am writing to submit my application for the Geoffrey Ogram Memorial Research Grant (GOMRG) 2025 competition. Our study, Pre-PLaN ("*Predictive Variables for Pathological Complete Response in Resectable NSCLC*"), leverages a unique, prospective dataset from patients with resectable non-small cell lung cancer (NSCLC) treated with neoadjuvant chemo-immunotherapy at London Health Sciences Centre Research Institute (LHSCRI).

This proposal focuses on integrating complementary, minimally invasive biomarkers, to predict pathologic complete response (pCR):

- Radiomics from PET/CT imaging
- Circulating tumor DNA (ctDNA)

Pre-PLaN is a prospective cohort study of patients with early-stage lung cancer undergoing neoadjuvant chemo-immunotherapy. The primary goal is to develop a predictive model of treatment response integrating clinical, radiologic, molecular, and ctDNA dynamics data. This includes collaboration with Guardant Health for circulating tumor DNA assays.

The novelty of the Pre-PLaN study lies in our integrated approach of combining clinical, radiomics, and ctDNA kinetics to predict pathological complete response (pCR). Our team believes this project aligns strongly with the GOMRG priorities of reducing the burden of lung cancer and optimizing patient care by advancing early detection with blood-based testing (i.e. ctDNA) and providing actionable insights for personalizing lung cancer treatment and follow-up strategies in Canadian patients. Based on the results of this study, we will plan a larger interventional study to further validate the predictive model and ultimately to choose treatment based on the results of the predictive model.

I am requesting $25,000 CAD in support to fund imaging analysis and statistical support. These elements are critical to the integrative scope of the project and are not covered by other funding sources already obtained for the study.

This project will generate insights that improve patient stratification, quality of care, and survival outcomes in resectable NSCLC, while shedding light on the biological underpinnings of lung cancer in early-stage resectable lung cancer. Thank you for your consideration.

Sincerely,
Dr. Saurav Verma
Medical Oncologist, Verspeeten Family Cancer Centre, London Health Sciences Centre (LHSC)
Assistant Professor and Clinician-Researcher, Department of Oncology, LHSCRI and Western University
London, ON, Canada

Summary of Proposed Research

Title: Predictive Variables for Pathological Complete Response in Resectable NSCLC (Pre-PLaN)

Background: Lung cancer remains the leading cause of cancer-related mortality in Canada. For resectable non-small cell lung cancer (NSCLC), neoadjuvant chemo-immunotherapy followed by surgery has emerged as a new standard of care based on trials such as CheckMate 816, which demonstrated markedly improved rates of pathologic complete response (pCR) and overall survival compared to chemotherapy alone (Figure 1) (1). However, not all patients benefit equally, and some experience no response or early relapse despite initial treatment response (2).

Two promising, minimally invasive biomarkers, radiomics (quantitative imaging features from PET/CT) and circulating tumor DNA (ctDNA), offer the potential to predict responses and recurrence earlier than conventional imaging or pathology alone (3–8). Preliminary studies suggest that radiomics signatures and ctDNA clearance after neoadjuvant therapy correlate with pCR and long-term outcomes (3,9–13), but data integrating both modalities remain limited.

Given the availability of a prospective cohort of resectable NSCLC patients already treated with neoadjuvant chemo-immunotherapy at our centre, we have a unique opportunity to rapidly evaluate radiomics and ctDNA as early detection and prognostic tools within a 12-month timeframe.

Objectives:

- **Primary:** To identify and validate multimodal predictors of pCR in patients with resectable NSCLC treated with neoadjuvant chemo-immunotherapy, and to integrate these into a predictive model.
- **Secondary:** To explore novel biomarkers including ctDNA, and advanced imaging radiomics as predictors of pCR and recurrence. Additional goals include assessing whether post-treatment PET response or liquid biopsy for minimal residual disease (MRD) can serve as non-invasive surrogates for pCR and early relapse detection.

Methods:

Design and Setting: Pre-PLaN is a prospective, single-centre cohort study enrolling 30 patients with resectable stage IB–IIIA NSCLC at the Verspeeten Family Cancer Centre at LHSC. All patients will receive standard-of-care neoadjuvant immunotherapy combined with platinum-doublet chemotherapy, followed by surgery (Figure 2 – Study schema).

Study Population: Eligible patients will be ≥18 years with ECOG 0–2 and no known EGFR, ALK, or ROS1 alterations. Both smokers and never-/light-smokers will be included, enabling analyses across demographic subgroups.

Data Collection: Comprehensive data will be obtained at baseline, during treatment, after three cycles of therapy, and post-surgery. Domains include:

- ***Clinical/demographic*:** age, sex, smoking status, comorbidities, ECOG status, vaccination status, and quality-of-life assessments (EORTC QLQ-C30, EQ-5D-5L).
- ***Radiology*:** CT volumetrics, PET SUV uptake, radiomic feature extraction, and sarcopenia index.
- ***Blood-based biomarkers*:** Complete blood counts, neutrophil/lymphocyte ratio, tumor markers, and serial ctDNA (provided in-kind by Guardant Health).

- ***Pathology*:** Tumor histotype, PD-L1 expression, next-generation sequencing (including TMB and STK11).

Data analysis:

- Radiomics feature extraction using standardized pipelines.
- ctDNA analysis for mutant allele fraction and clearance dynamics at predefined time points.
- Univariable analyses to identify candidate features associated with pCR.
- Multivariable modeling (LASSO logistic regression, random forest) to develop a combined predictive model; model performance evaluated by ROC AUC, calibration, and cross-validation.
- Exploratory analysis of early recurrence prediction using 6 and12-month imaging and ctDNA data.

Timeline (January - December 2026)

Timeframe	**Study Milestones**
January - March	Radiomics segmentation & feature extraction; remaining ctDNA collection and assays completed.
April - June	Data cleaning, harmonization, preliminary analyses.
July - September	Model building for pCR prediction; interim results review.
October - December	Final analyses; abstract submission to a Lung Cancer Conference; manuscript drafting; final report to Lung Cancer Canada.

Feasibility

- 25/30 patients already enrolled with imaging and ctDNA samples largely collected.
- Radiomics expertise and bioinformatics support available at Western University.
- ctDNA assays will be performed via established collaboration with Guardant Health.
- All analyses and reporting achievable within 12 months (Jan - Dec 2026).

Expected Outcomes:

- Development of integrated predictive models for pCR with clinical utility.
- Validation of ctDNA and radiomics as non-invasive predictors of response and recurrence.
- Creation of a unique biobank and data repository for future lung cancer research.

Significance: The Pre-PLaN study will generate insights to directly guide treatment in resectable NSCLC. Predictive models will identify patients most likely to benefit from neoadjuvant immunotherapy. Analyses of ctDNA and radiomics will advance understanding of lung cancer biology, particularly in non-smokers. As a systems-level "test run," the study will also optimize neoadjuvant pathways. Ultimately, Pre-PLaN will accelerate biomarker translation, improve patient selection and patient outcomes.

Impact Statement

This project directly addresses the GOMRG priorities of early detection and understanding disease etiology in diverse populations by leveraging complementary, minimally invasive biomarkers to enable real-time prediction of treatment response and recurrence risk in patients with resectable non-small cell lung cancer (NSCLC). Through the Pre-PLaN study, we will integrate radiomic, molecular, and circulating tumor-derived biomarkers into predictive models that resolve clinical uncertainty surrounding response and toxicity to neoadjuvant chemo-immunotherapy. This comprehensive approach will equip clinicians with tools to identify patients most likely to benefit from treatment, while also uncovering novel risk factors and biological mechanisms underlying tumor behavior across never-smokers, light-smokers, smokers, and other diverse patient populations.

Importantly, this research could transform both surgical and adjuvant decision-making. For example, patients predicted to achieve a pathological complete response (pCR) might avoid surgery altogether, while those achieving partial response but unlikely to relapse after resection could safely forgo adjuvant therapy and its associated toxicity. These capabilities represent a major step toward tailoring treatment intensity to individual patient risk and likelihood of benefit, ultimately reducing unnecessary harm and optimizing survival outcomes.

The inclusion of circulating tumor DNA and advanced imaging will accelerate early detection of resistance and recurrence, enabling clinicians to intervene earlier than with current standards. In the short-to-medium term, Pre-PLaN will generate actionable knowledge that can be rapidly translated into optimized care pathways and prospective clinical trial design. Ultimately, this work has the potential to transform the management of resectable NSCLC by enabling biomarker-driven, personalized strategies that reduce mortality, limit treatment-related toxicity, improve quality of life, and exert a sustained influence on lung cancer research and patient outcomes in Canada and beyond.

Public (Non-Scientific) Summary

Lung cancer is one of the leading causes of cancer-related deaths in Canada. Even when it is detected early and surgically removed, many patients still face the risk of the cancer returning. Currently, doctors have limited ways to predict which patients will respond well to additional treatments, such as chemotherapy or immunotherapy, and which patients might safely avoid them. This uncertainty can lead to unnecessary side effects or missed opportunities for more targeted care.

Our project aims to change this by developing new, minimally invasive ways to monitor lung cancer after chemo-immunotherapy and/or surgery, by guiding personalized treatment decisions. We are combining two advanced approaches: a blood test that detects tiny fragments of tumor DNA circulating in the bloodstream, and sophisticated imaging analysis, called radiomics, which extracts detailed patterns from standard CT and PET scans. While the blood test provides a real-time snapshot of the tumor's presence, the imaging reveals subtle changes in the tumor and surrounding tissue that are not visible to the naked eye. Together, these tools can give doctors an early and accurate picture of how a patient's cancer is responding to treatment and the risk of it returning.

For example, a patient whose tests suggest that some cancer may still be present after surgery could receive additional therapy sooner, improving the chances of long-term survival. Conversely, a patient whose tests indicate a low risk of recurrence could avoid unnecessary treatment and its side effects. This personalized approach has the potential to improve outcomes, reduce harm from overtreatment, and provide peace of mind for patients and families.

The insights gained from this project will also help guide future clinical trials, improving how new treatments are tested and implemented. In the long term, this research could transform the management of resectable (i.e., removal via surgery) lung cancer, moving toward care that is guided by precise, personalized information rather than a one size fits all approach.

Ultimately, our goal is to improve survival and quality of life for patients with lung cancer. By using cutting-edge blood and imaging tests, we hope to detect recurrence earlier, tailor treatments to individual patients, and reduce unnecessary side effects. This research represents an important step toward a future where treatment for lung cancer care is safer, smarter, and more personalized.

Budget and Justification

Total requested: $25,000 CAD

Item	Cost in CAD
Radiomics collaboration - Data scientist - Image Segmentation - Image Feature Extraction & QC	 $10,000 $3,720 $6,280
Cancer Detection and MRD Assay	In-kind support from Guardant Health
Phlebotomy, plasma processing, storage and handling	Departmental seed funding for Pre-PLaN study
Research coordinator	Departmental seed funding for Pre-PLaN study
Biostatistics and data management (Statistical modeling, cross-validation, ROC/AUC calculation, and final report generation)	$5,000
Total Requested	$25,000

Budget Details:

- **Imaging/radiomic analysis (LHSCRI): $20,000**
  - Data scientist = $80/hour*125 hours
  - Image segmentation = $62/image*30 patients*2 timepoints
  - Image feature extraction as well as quality control = $105/image*60 images
- **Biostatistics and data management ($100/hour*50 hours): $5,000**
  - Biostatistician to perform statistical modeling, cross-validation, ROC/AUC calculation, and final report generation

Other support:

- Phlebotomy, plasma processing, storage and handling as well as research coordination are covered by Departmental seed funding already obtained for Pre-PLaN study.
- Guardant Health provides in-kind support for ctDNA assays.
- LHSC/LHSRI supports biobanking and data infrastructure.

Justification: The requested funds fill a critical gap in the project. Without GOMRG support, we will be unable to perform the advanced radiomic analyses that distinguish this project and directly address the grant's focus on early blood-based detection (i.e. ctDNA funded in-kind by Guardant Health) and etiology. The funds will not be used for infrastructure or indirect costs, ensuring that all resources directly support the proposed research.

Names of the investigator(s)
Principal Investigator (PI): Saurav Verma
Co-PI: Mark Vincent

Appendix 1 – Figures

Figure 1 – Overall survival with neoadjuvant chemo-immunotherapy in CheckMate 816 trial (1)

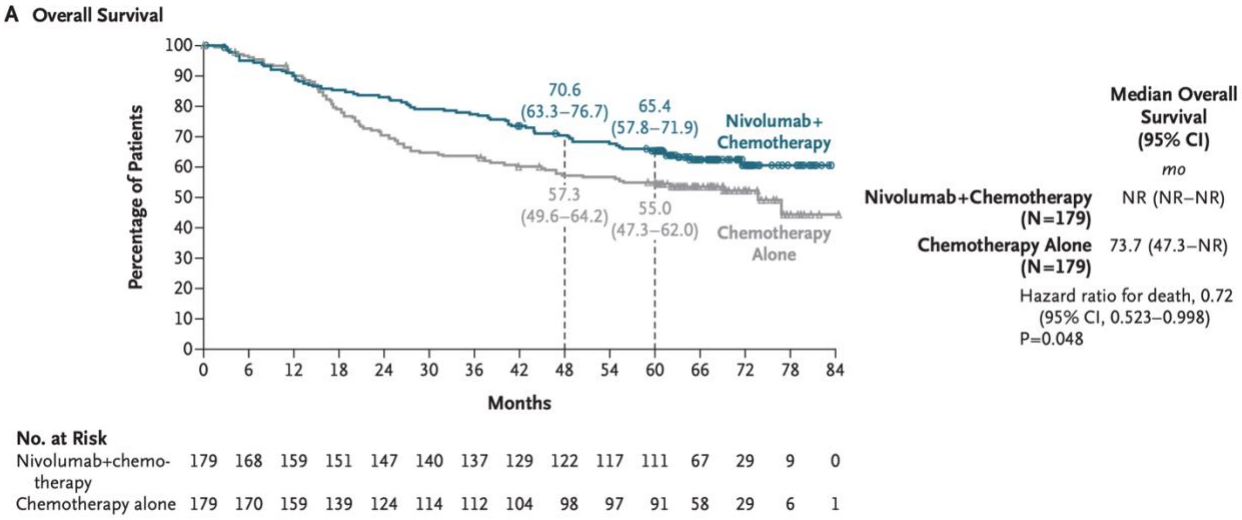
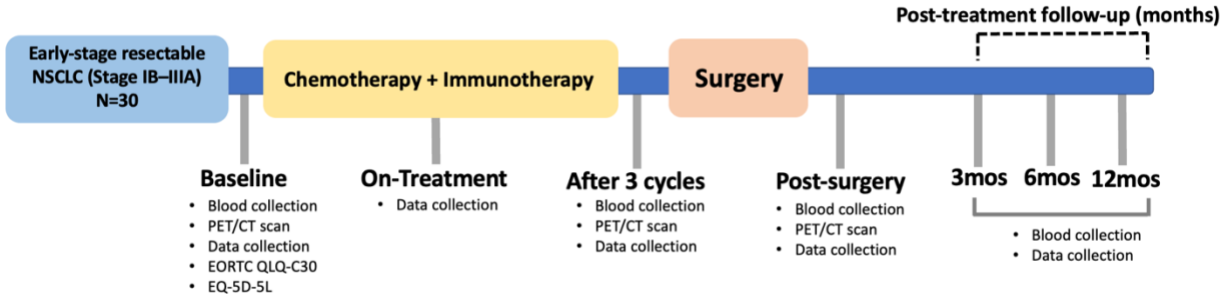


Figure 2 – Pre-PLaN study schema



Appendix 2 – References

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London Health Sciences Centre
Research Institute

September 24, 2025

RE: Geoffrey Ogram Memorial Research Grant

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To the Reviewing Panel,

I am pleased to express my strong support for the grant proposal to the Geoffrey Ogram Memorial Research Grant, titled *"Predictive Variables for Pathological Complete Response in Resectable NSCLC (Pre-PLaN)*".

Dr. Saurav Verma, Assistant Professor in the Department of Medical Oncology, is the principal investigator of this study. As Interim Vice President of Research and London Health Sciences Centre Research Institute Scientific Director, I can assure you that the necessary administrative, communications, external relations, and finance support will be provided, along with the required infrastructure, for the duration of the proposed research.

London Health Sciences Centre Research Institute (LHSCRI), the research institute of London Health Sciences Centre (LHSC), offers extensive research space, including facilities adjacent to the Verspeeten Family Cancer Centre (VFCC), and a full range of financial, contractual, and regulatory expertise that is available to investigators. Clinical research excellence is supported by a comprehensive training program for all personnel involved with human research subjects, ensuring competence in regulatory requirements, record keeping, and study conduct. LHSCRI researchers are further supported by dedicated clinical trial facilities, including one specifically for cancer studies. These resources have contributed to LHSCRI's growth as one of the largest hospital-based research institute in Ontario and in Canada, based on annual research expenditure.

The VFCC sees and treats over 30–50 patients with resectable NSCLC annually. This centre offers state-of-the-art facilities and resources that will be fully utilized for the proposed research.

I am confident that this study will have a meaningful impact on the use of radiomics and liquid biopsy for early detection and monitoring of recurrence for patients with early-stage lung cancer. For these reasons, LHSCRI is proud to provide full institutional support for this application.

Sincerely,

Dr. Chris McIntyre
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