RESEARCH Matters

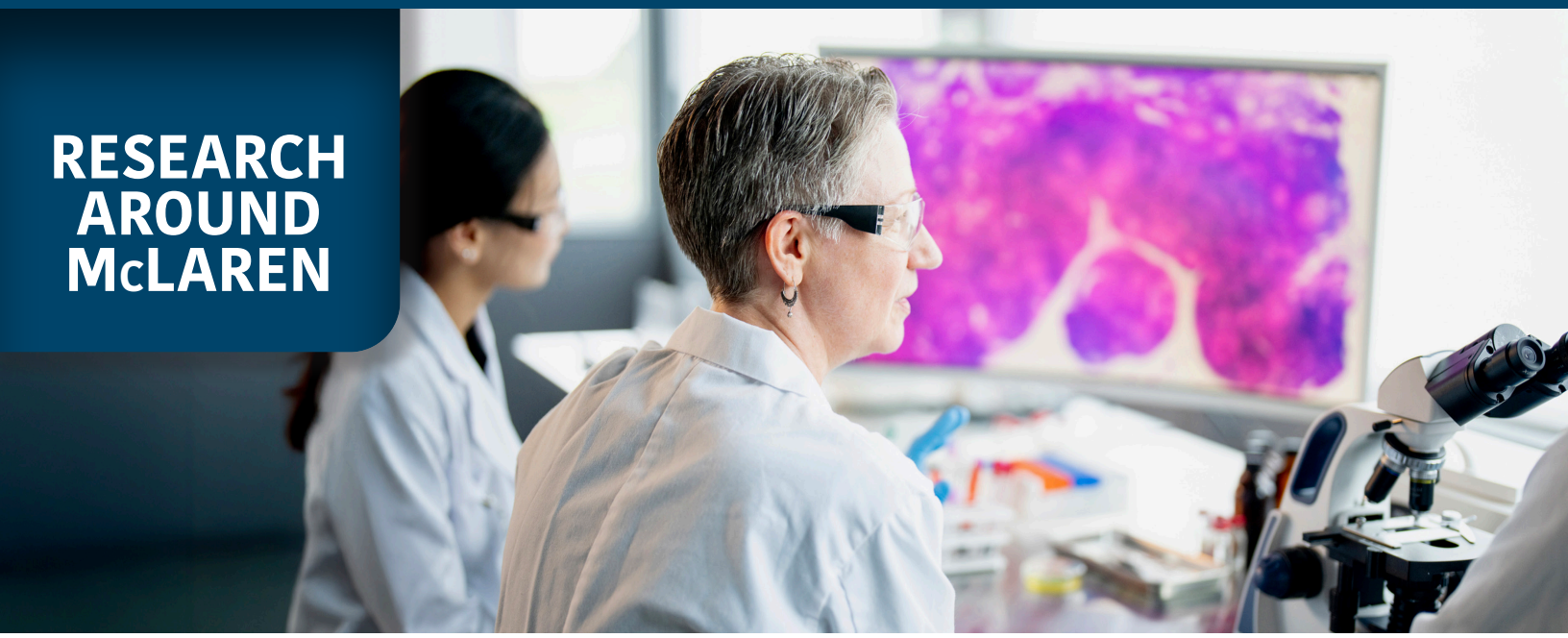
Winter 2026

IN THIS ISSUE

Association for the Accreditation of Human Research Protection Programs, Inc.
Full Accreditation

McLaren

RESEARCH AROUND McLAREN



KARMANOS AND MCRI LAUNCH FIRST JOINT ONCOLOGY/NON-ONCOLOGY STUDY

STRENGTHENING CLINICAL TRIAL COMMUNICATION

The Karmanos Cancer Network and the McLaren Center for Research and Innovation (MCRI) have officially partnered on their first collaborative research study spanning both oncology and non oncology research sites. The project, Ask Questions About Clinical Trials (ASQ CT), marks a major milestone in the integration of research efforts across the McLaren system and reflects a shared commitment to improving patient-centered communication about clinical trials.

Led by **Lauren Hamel, PhD, MBA**, Associate Professor of Oncology at Wayne State University and Co-Leader of Population Studies Research Program at Karmanos, the ASQ CT study aims to strengthen how providers discuss clinical trials with patients and how patients participate in those conversations. This project is funded by the McLaren Research Foundation.

Lauren Hamel, PhD, MBA

Why This Study Matters

High-quality communication between patients and providers is a cornerstone of effective care. Research consistently shows that when patients feel informed, heard, and engaged, they experience better outcomes, greater satisfaction, and improved trust in their care team. These communication needs become even more critical when discussing clinical trials, where information is complex and decisions can feel overwhelming.

Despite the importance of clinical trials, enrollment remains low across the research industry nationwide. Many trials across cancer, cardiovascular disease, and other conditions struggle to accrue enough participants to answer essential scientific questions. Poor communication is a known contributor to low enrollment.

The ASQ CT study addresses this challenge directly.

The Intervention: A Question Prompt List (QPL) for Clinical Trials

The ASQ CT brochure is a Question Prompt List (QPL). This is a structured, patient-friendly tool that encourages individuals to ask questions, express concerns, and participate actively in treatment discussions. QPLs have been tested extensively in oncology and other medical settings, demonstrating improvements in:

- Patient knowledge and confidence
- Quality of information exchanged
- Shared decision making
- Clinical trial invitations and discussions
- Psychosocial outcomes such as anxiety and distress

The ASQ CT brochure adapts this proven approach specifically for clinical trial conversations across multiple specialties.

A First of Its Kind Collaboration

What makes this study historical for McLaren is its system-wide scope. For the first time, Karmanos network oncology sites and MCRI non-oncology sites will enroll patients in the same research study, creating a unified effort across specialties and locations.

Participating locations include nine Karmanos sites and the five MCRI sites. The locations represent cardiology, neurology, oncology, and other non-oncology specialties. This cross-disciplinary design reflects the growing recognition that clinical trials and communication challenges surrounding them are present across therapeutic areas.

The study will seek to recruit over 200 patients who are being considered for a clinical trial. Participants will receive the ASQ CT brochure and complete brief surveys before and after their clinical visit to assess communication quality, self-efficacy, knowledge, distress, trust, and whether clinical trials were discussed or offered.

Evaluating Impact Across the System

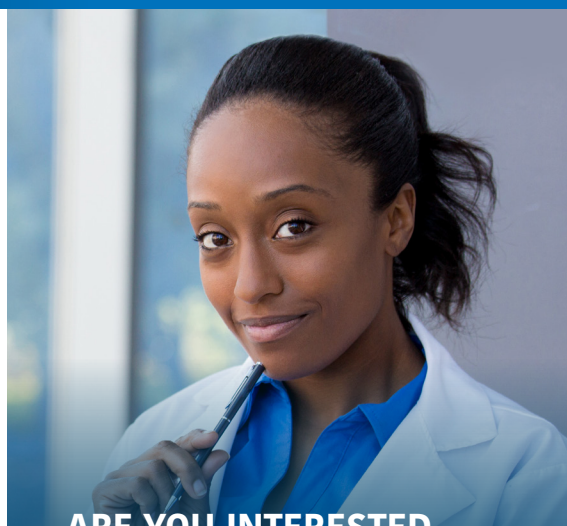
Using the RE AIM framework, the study will evaluate:

- **Reach:** Who participates and how representative they are.
- **Effectiveness:** Impact on communication and patient reported outcomes.
- **Adoption:** How many clinics implement the intervention.
- **Implementation:** Feasibility and consistency across sites.
- **Maintenance:** Potential for long-term integration.

This approach ensures that findings will inform not only research practice but also clinical operations across the McLaren system.

Looking Ahead

This project represents a significant step forward in unifying research efforts across McLaren Health Care. By improving how clinical trials are discussed, the study has the potential to strengthen trial accrual, enhance patient experience, and advance equitable access to research opportunities across both oncology and non-oncology care.



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

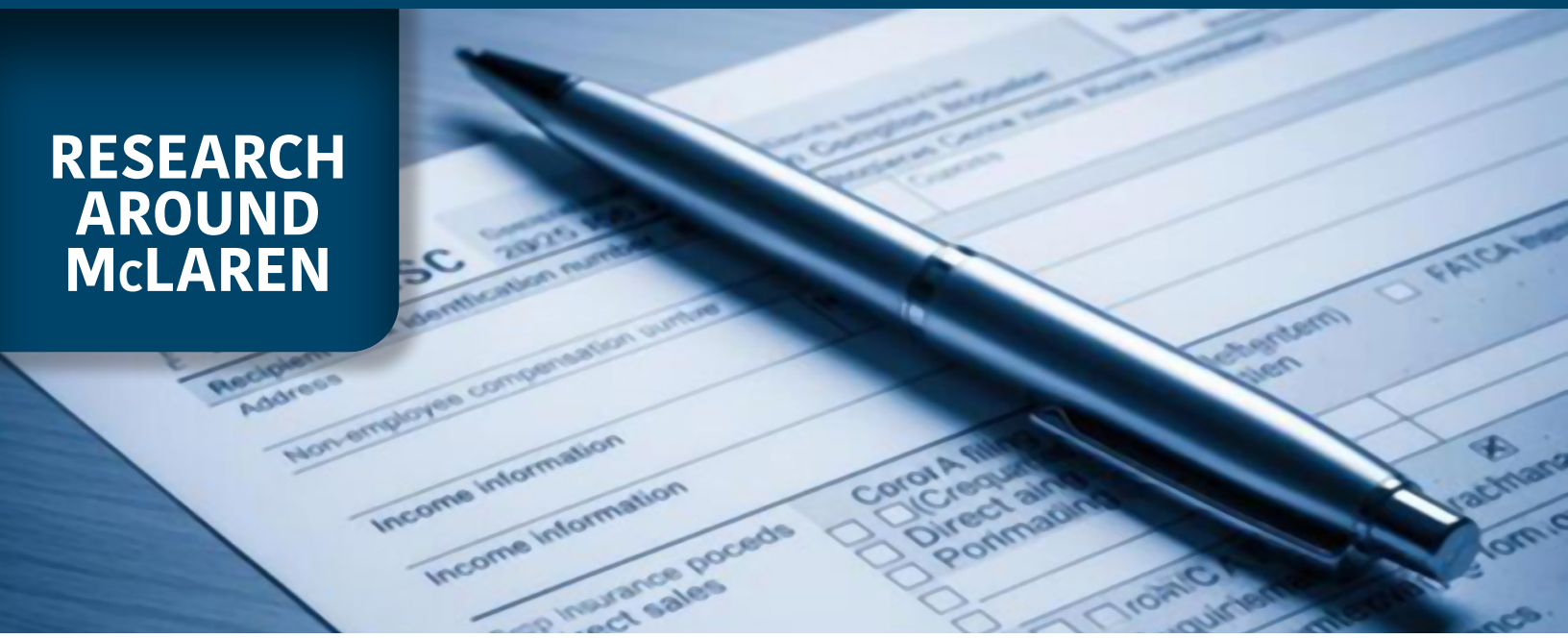
For information on enrolling in a clinical trial, please visit **mclaren.org/main/clinical-research-trials**. Here you will find a list of open-enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- Diabetes
- Orthopedic Surgery
- COVID-19
- High Blood Pressure (Hypertension)
- Stroke
- Heart Attacks / Heart Failure / Heart Disease
- Kidney Diseases
- Lung Diseases
- Peripheral Artery Disease
- Carotid Artery Disease
- Mastectomy
- Various Cancers
  - Breast
  - Lung
  - Prostate
  - Multiple Myeloma
- Patients who underwent intracranial aneurysm coiling
- Drug study for patients with recent acute coronary syndrome

For a complete list of conditions, please visit our website listed above.

RESEARCH AROUND McLAREN



IRS INCREASES 1099 REPORTING THRESHOLD

WHAT THIS MEANS FOR RESEARCH PARTICIPANT PAYMENTS

Beginning January 1, 2026, the IRS has increased the reporting threshold for certain payments, including research participant stipends, from $600 to $2,000 per calendar year. This change represents the first major adjustment to the threshold in decades and has meaningful implications for research sites, investigators, and participants.

Although the reporting threshold has increased, one important fact remains the same: the research participant compensation is still considered taxable income. Institutions must issue a Form 1099-MISC to any participant who receives $2,000 or more in a calendar year, and participants are responsible for reporting this income on their tax returns.

Why the Change Matters

For years, the $600 threshold created administrative challenges for research sites and unintended barriers for participants. Many individuals, particularly those from lower income communities, expressed concern about receiving a 1099 for modest stipends, which sometimes discouraged participation in research.

Increasing the threshold to $2,000 reduces the number of participants who will receive a 1099 and eases administrative workload for research teams. It also helps ensure that stipends function as intended: to compensate participants fairly for their time, effort, and inconvenience, and not to create unnecessary financial stress.

Ethical Considerations: Fairness, Equity, and Undue Influence

Compensating research participants is not only a logistical matter but also an ethical one. Stipends must strike a balance between:

Fair Compensation

Participants should be compensated for the time, inconvenience, and burdens associated with research participation. Appropriate compensation supports equity by ensuring that participation is not limited to those who can afford unpaid time.

Avoiding Undue Influence

Payments should not be so high that they pressure individuals to participate against their better judgment or overlook risks. The increased IRS threshold does not change how stipends should be set. It only changes when reporting is required.

Transparency in Consent

Consent forms must clearly explain how much participants will be paid and how those payments will be distributed.

Looking Ahead

The increased threshold represents a positive shift for both research participants and research operations. It reduces administrative burden, supports equitable participation, and aligns tax reporting requirements more closely with the realities of modern research.

NEW NON-ONCOLOGY RESEARCH OFFICE AT McLAREN FLINT

MCRI is thrilled to announce that the non-oncology research office at McLaren Flint has moved to a new location. Formerly known as the Emergency Department Fast Track space on 2 Central, MCRI has found a new, comprehensive home. Complete with patient waiting space, private exam spaces, lab draw and processing area, administrative offices, drug and device storage and meeting and monitoring space, the new Flint MCRI location is ready to serve the local clinicians and patients.

We encourage local clinicians to stop by and view our hallway display or come inside for a chat with a research coordinator to learn about what we do and how to get involved. McLaren Flint's current portfolio has openings for new clinical trials, and we are equipped to coordinate and manage trials in most therapeutic areas. Our experienced staff can walk you through the process of becoming a qualified investigator, and you'll find a checklist of the initial "to-do's" on our hallway display, or listed below for your reference:

1. Provide a hand signed and dated current CV
2. Provide a list of areas of interest within your therapeutic area and/or a list of studies you have participated in.
3. Create an account at www.citiprogram.org
   a. Complete Biomedical Research Basic Course
   b. Complete MHC Conflict of Interest Course
   c. Complete GCP for Clinical Investigations of Drug and Devices (FDA) Course
4. Email documents or certificates to MCRI@mclaren.org or drop off at the research office on 2C.

Ready to get started? Talk to local drug or device representatives about what clinical trial opportunities might be available with the products you currently

CONTINUED ON PAGE 6

NEW NON-ONCOLOGY RESEARCH OFFICE

CONTINUED FROM PAGE 5

use. Touch base with colleagues at other institutions to see what clinical trials they might have going and ask them to recommend McLaren as a potential site. Attend conferences and join online communities to let industry partners know that you're interested and have local resources available to conduct clinical trials.

Still not sure? Stop by MCRI on 2C, enjoy a snack with our staff and get inspired by our new space!

McLaren Center for Research and Innovation at McLaren Flint, located on 2C outside the Emergency Department, is open Monday through Friday, 7 a.m. - 4 p.m. Please note, due to the storage of confidential information, FDA regulated test articles and other highly sensitive material, the doors will be locked when staff are not present. If we are attending to patients on the floor and miss your visit, please drop a card or note in the drop box outside and we will get in touch! We look forward to expanding research throughout the hospital and the opportunity to offer exciting and innovative treatment options to more of our patients.

If you have questions or would like additional information, please email **MCRI@mclaren.org**.

DO YOU HAVE A RESEARCH PROJECT THAT NEEDS FUNDING?

McLaren Health Care has formed a corporate level Research Funding Committee. This committee has been created to establish a system-wide strategic plan and process for awarding research funding to investigators. One goal of this committee is to support and strengthen investigator-initiated research within the corporation. Awards of up to $5,000 will be awarded to individuals involved in Graduate Medical Education Research (Residents and Fellows). Awards of up to $20,000 will be awarded to non-GME individuals interested in pursuing investigator-initiated research. Non-GME awards are open to all McLaren employees or affiliated providers. These funds are to be used for the conduct of the observational or interventional research study and will be awarded on a quarterly basis. Due dates for application submissions are January 1, April 1, July 1, and October 1 of each year. The application process can be accessed at **www.mcLaren.org/fundingapplication**. Required information for the application includes a detailed description of the research project, as well as a proposed budget.

INVESTIGATOR RESOURCES

McLaren Research Administration and Research Integrity
mclaren.org/main/research

CITI Training, Biomedical, GCP
citiprogram.org

SOCRA
socra.org

ACRP
acrp.org

Health and Human Services
hhs.gov/programs/research

FDA Guidance for Industry: Investigator Responsibilities
fda.gov/media/77765/download

FDA Guidance for Sponsor-Investigators
fda.gov/media/92604/download

GCP Regulations
fda.gov/science-research/clinical-trials-and-human-subject-protection/regulations-good-clinical-practice-and-clinical-trials

Code of Federal Regulations
ecfr.gov/current/title-21

- 21 CFR 312 – Investigational New Drug Application
- 21 CFR 812 – Investigational Device Exemptions
- 45 CFR 46 – Protection of Human Subjects

Clinical Trials.gov
clinicaltrials.gov

IRB Consultations
https://www.mclaren.org/main/irb-consultations

RESEARCH AROUND McLAREN

KARMANOS FIRST IN MICHIGAN TO OFFER LIFILEUCEL (TIL THERAPY) TO TREAT ADVANCED MELANOMA

Over the last decade, melanoma survival rates have improved significantly due to ongoing research and the development of immunotherapy. Lifileucel, also known by its brand name AMTAGVI, is a new form of immunotherapy approved by the U.S. Food and Drug Administration (FDA) for patients with metastatic melanoma whose cancer has stopped responding to immune checkpoint inhibitors. The Barbara Ann Karmanos Cancer Institute is the first and only cancer center in Michigan to treat a patient with this new immunotherapy.

Yusra Shao, MD

"I am truly excited for our patients. We have a new promising treatment, giving them hope in their melanoma treatment journey," said Yusra Shao, MD, medical oncologist and leader of the Cutaneous (Skin) Oncology Multidisciplinary Team.

What is TIL Therapy?

Tumor-infiltrating lymphocyte (TIL) therapy is a one-time treatment for adults who have melanoma that cannot be treated with surgery, and the disease has progressed following previous therapy, including an immune checkpoint inhibitor and BRAF-targeted therapy (if BRAF-mutated). The treatment is most successful when given to patients early in their care plan.

The TIL Treatment Process

The treatment is unique for each patient because no two patients have the same cell makeup. The process begins with the removal of a small portion of the tumor, which is sent to a laboratory for extraction and expansion of T-cells (immune cells) obtained from the tumor.

"You can look at it as if we're giving you a treatment made by you. We take the patient's immune cells and grow them in the lab, where they become stronger and smarter," Dr. Shao said. "After the extraction, the patient is given chemotherapy for a week to empty out the bone marrow for new immune cells to take home."

After chemotherapy, the prepared TILs, now with stronger immune cells that were grown in the lab, are infused back into the patient intravenously (IV).

"After the patient receives the TIL therapy, they are given a medication called IL-2. IL-2 is a chemical that our body naturally makes," said Dr. Shao. "This chemical tells the new immune cells that it's now time to get to work."

TIL therapy involves a two-week process, from chemotherapy to TILs infusion, followed by IL-2 administration, all of which are performed in the hospital. Patients are monitored closely throughout the process and after they have completed the treatment.

This treatment was approved based on a clinical trial that included 73 patients whose cancer had progressed on multiple prior therapies. After receiving

TIL therapy, 31% of patients experienced tumor shrinkage, and in another 46% the cancer stopped growing. Half of the responses were seen after six weeks of receiving the treatment. In patients whose cancer shrank, the cancer remained under control on average for three years.

"For patients with progressive disease after checkpoint inhibitors and targeted therapy, these results represent a major advancement and a new life," said Dr. Shao.

TIL therapy requires a multidisciplinary approach, involving multiple teams at Karmanos: the Cutaneous Oncology and Bone Marrow and Stem Cell Transplant MDTs, surgical oncology, and pharmacy team members. Patients also have access to a patient navigator and social worker.

KARMANOS LISTED AMONG 2025 BEST ONCOLOGY PROGRAMS IN UNITED STATES

The Barbara Ann Karmanos Cancer Institute has been included on the 2025 list of 100 Hospitals and Health Systems with Great Oncology Programs compiled by Becker's Hospital Review. The Detroit headquarters anchors one of Michigan's largest cancer networks, the Karmanos Cancer Network.

Becker's list includes the premier providers of cancer care from across the country, many of which are National Cancer Institute (NCI)-Designated Comprehensive Centers. World-renowned experts lead the oncology programs, which provide novel treatments, conduct leading-edge research, offer innovative therapies and transformative clinical trials, all while upholding stringent safety standards to improve patient outcomes.

The Karmanos headquarters in Detroit has been an NCI-Designated Comprehensive Cancer Center since 1978, making it the first in Michigan to receive this recognition and the only NCI-designated center in metro Detroit. As McLaren Health Care's oncology service line, Karmanos is at the forefront of developing and translating scientific knowledge from promising laboratory discoveries into new treatments. Cancer patients at Karmanos and at Cancer Network locations throughout Michigan receive an unmatched, comprehensive approach, including access to therapies exclusively available at Karmanos, innovative care, cancer prevention programs, and multidisciplinary teams of cancer specialists.

From groundbreaking research to the most up-to-date therapies and individualized treatment plans, Karmanos is leading the fight against cancer. At any given time, the Institute is running hundreds of cancer-specific scientific investigations and active clinical trials aimed at providing better treatments for more than 200 known cancers.

A leading health care industry outlet, the Becker's Hospital Review editorial team accepted nominations and examined rankings from reputable organizations, such as U.S. News & World Report and Newsweek, while compiling the list. The list aims to highlight oncology programs that are at the forefront of their field.

CLINICAL TRIALS CONNECT

Karmanos and McLaren offer studies across a range of cancer types, offering our patients access to innovative treatments and research-driven care. Here are just a select number of actively recruiting trials.

We encourage you to explore the full list of available trials using the Karmanos Cancer Institute Clinical Trials App, a convenient tool to search by cancer type, eligibility, therapy, and more. You may also visit **karmanos.org/trialsportal**.

Download the Karmanos Clinical Trials APP at **karmanos.org/clinicaltrials** or scan the QR code.

If you have questions, problems, or concerns regarding the app, email **informatics@karmanos.org**.

Clinical Trial
LUNG CANCER

PHASE III

Principal Investigator:
Dipesh Uprety, MD

Karmanos Trial ID:
2024-101

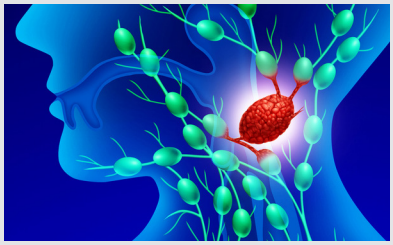
Age Group:
Adult

Locations Available:
- Detroit
- Farmington Hills
- Flint
- Lansing

Therapies:
- Chemotherapy
- Immunotherapy

Drugs:
- Carboplatin
- Nab-paclitaxel
- Pemetrexed
- Ivonescimab
- Pembrolizumab
- Paclitaxel

Eligibility Criteria:
- Metastatic (stage IV) non-small cell lung cancer.
- Must have a TPS or TC for PD-L1 expression.
- At least one measurable noncerebral lesion.
- No prior systemic treatment for metastatic non-small cell lung cancer.



Clinical Trial
NON-HODGKIN LYMPHOMA

PHASE III

Principal Investigator:
Dipenkumar Modi, MD

Karmanos Trial ID:
A052101

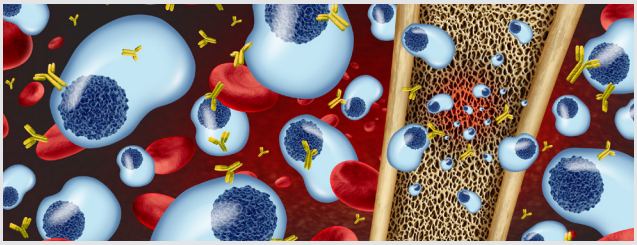
Age Group:
Adult

Locations Available:
- Bay City
- Detroit
- Flint
- Mt. Pleasant
- Clarkston
- Farmington Hills
- Lapeer
- Petoskey

Therapies:
- Biological Therapy
- Immunotherapy

Drugs:
- Rituximab
- Zanubrutinib

Eligibility Criteria:
- Histologically confirmed mantle cell lymphoma.
- Presence of either measurable disease or bone marrow involvement.
- No prior systemic treatment for mantle cell lymphoma.
- No prior exposure to a BTK inhibitor or anti-CD-20 monoclonal antibody.



Clinical Trial
MULTIPLE MYELOMA

PHASE II

Principal Investigator:
Andrew Kin, MD

Karmanos Trial ID:
2024-062

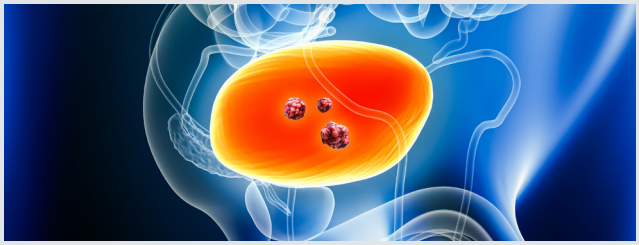
Age Group:
Adult

Locations Available:
- Detroit
- Farmington Hills
- Flint
- Lansing

Therapies:
- Biological Therapy

Drugs:
- Dexamethasone
- Teclistamab

Eligibility Criteria:
- Histologically confirmed multiple myeloma that is exposed, relapsed, or intolerant to one of each of the following classes of agents:
  a. A proteasome inhibitor;
  b. An immunomodulatory drug;
  c. An anti-CD38-monoclonal antibody.
- Must have received between 1-4 lines of prior systemic therapy.
- Measurable disease, defined as one of the following:
  a. M-protein ≥ 0.5g/dL;
  b. Urine M-protein (Bence-Jones protein) ≥ 200 mg/24 hours;
  c. Serum free light chain difference > 100 mg/L;
  d. Biopsy-proven plasmacytoma.
- ECOG performance status of 0-2.



Clinical Trial
UROTHELIAL CANCER

PHASE II/III

Principal Investigator:
Yusra Shao, MD

Karmanos Trial ID:
A032103

Age Group:
Adult

Locations Available:
- Bay City
- Detroit
- Farmington Hills
- Lansing
- Petoskey

Therapies:
- Biological Therapy
- Immunotherapy

Drugs:
- Nivolumab
- Relatlimab

Eligibility Criteria:
- Histologically confirmed urothelial cancer of the bladder, urethra, ureter, or renal pelvis.
- Radical surgery (i.e., cystectomy, nephroureterectomy, or ureterectomy) ≥ 3 weeks, but ≤ 12 weeks prior to pre-registration.
- No evidence of residual cancer or metastases after surgery.
- Available tumor tissue from radical surgery must be available for “central” Signatera testing submitted at pre-registration.

RESEARCH AROUND McLAREN

KRAS "CRACKED OPEN"

KARMANOS RESEARCHERS PUBLISH HIGH-IMPACT REVIEW NOW RANKED AMONG THE MOST-READ IN ITS FIELD

Over the last decade, melanoma survival rates have improved significantly due to ongoing research and the development of immunotherapy. Lifileucel, also known by its brand name AMTAGA, major new review published in the high-impact Nature journal *Signal Transduction and Targeted Therapy* (impact factor >50) is reshaping the conversation around KRAS, one of the most historically "undruggable" oncogenes in human cancer. The article, "Targeting KRAS mutations: orchestrating cancer evolution and therapeutic challenges," led by researchers at the Barbara Ann Karmanos Cancer Institute and Wayne State University, has rapidly gained international attention, becoming one of the most accessed papers in the journal, earning an Altmetric score of 33, and being highlighted among the Top 10 oncology articles of the week by *OncoDaily News*; a clear sign of its scientific and clinical impact.

KRAS mutations lie at the heart of some of the world's deadliest malignancies, especially pancreatic ductal adenocarcinoma (PDAC), colorectal cancer and lung cancer. For decades, KRAS eluded every attempt at therapeutic targeting because its protein surface lacked exploitable binding pockets, cementing its reputation as "undruggable." Only in the last few years has that perception shifted, following the discovery of the switch-II pocket in KRAS-G12C and the development of the first direct inhibitors. While these drugs validated that KRAS can indeed be targeted, their modest response rates and limited durability highlight the need for next-generation strategies, especially for KRAS mutations prevalent in PDAC, such as G12D and G12V.

According to the corresponding author, Asfar Azmi, PhD, professor, director of Pancreas Cancer Research, and member of the Molecular Therapeutics (MT) Research Program, this article reflects a pivotal turning point for the field.

"For decades, KRAS symbolized everything we could not achieve in cancer therapy. This review makes it clear that the scientific landscape has undergone a fundamental shift. With advances in chemistry, structural biology, tumor immunology, and microenvironmental science, KRAS is now a tractable therapeutic target. The path forward lies in mutation-specific precision and rationally designed combinations that can deliver truly durable responses."

Dr. Azmi emphasized the ongoing translational efforts in his laboratory at Karmanos, where multiple combination strategies are currently under active investigation. These include pairing KRAS inhibitors with agents targeting proliferating cell nuclear antigen (PCNA), p21-activated kinase 4 (PAK4), and exportin-1 (XPO1). Each approach is designed to counter adaptive resistance pathways and deepen the magnitude and duration of KRAS inhibitor responses in pancreatic and other KRAS-driven malignancies. Together, these efforts aim to establish a next-generation therapeutic framework in

which KRAS inhibition becomes not only feasible but also meaningfully transformative for patients.

Khalil Choucair, MD, MSc, the first author of this review, medical oncologist, assistant professor of Oncology, member of the Thoracic Oncology, Phase I Clinical Trials Multidisciplinary Teams (MDT) and the MT Research Program, highlighted that the goal of this review was to provide a balanced, yet forward-looking synthesis of the field.

"G12C inhibitors proved the fundamental concept that direct KRAS targeting is possible. However, the next phase requires us to overcome resistance, broaden efficacy to these drugs, and integrate therapeutic strategies that reflect tumor evolution, lineage plasticity, and microenvironmental forces," he said. "The pace of progress in KRAS biology and drug development has never been faster, and this review captures both the momentum and the scientific maturity now driving the field forward. Such efforts, as summarized in our work, stand as proof of the power of research to advance clinical care and translate into new hope to our patients on their journey."

"A major fraction of the KRAS therapeutics discussed in this review, including KRAS-G12C inhibitors, emerging KRAS-G12D inhibitors, pan-RAS drugs, and KRAS-targeted vaccines, are already being offered or are available through clinical trials at Karmanos. We are not just analyzing the field, we are directly implementing the most advanced KRAS-targeted approaches in our patient population," explained Najeeb Al Hallak, MD, MS, medical oncologist, co-leader of the Gastrointestinal and Neuroendocrine Oncology MDT, and member of the Phase I Clinical Trials MDT and the MT Research Program.

"The fact that this review has become one of the most accessed papers in the journal, has earned a strong Altmetric score, and was featured among the Top 10 articles in *OncoDaily News* speaks to its importance," said Boris Pasche, MD, PhD, FACP, president and CEO of Karmanos. "It underscores Karmanos' leadership in translational oncology and our commitment to addressing the most challenging problems in cancer research. KRAS has been considered impenetrable for decades, and our team is now helping define the strategies that will change that."

Md. Hafiz Uddin, PhD, scientist, MT Research Program member at Karmanos, was also a contributing author.

As the field moves toward broad-spectrum KRAS inhibition, addressing G12D, G12V, and even pan-RAS signaling with RNA-based modalities, PROTAC degraders, immune-based approaches, and rationally designed combinations, the narrative around KRAS is undergoing a historic shift. Karmanos stands prominently at the forefront of this transformation, both through scholarship and through active clinical trials that are already reaching patients.

Find open gastrointestinal and neuroendocrine clinical trials available at Karmanos by visiting **karmanos.org/clinicaltrials**. Learn more about the Molecular Therapeutics Research Program at **karmanos.org/MT**.

Asfar Asmi, PhD

Khalil Choucair, MD, MSc

Al Hallak, MD, MS

Md. Hafiz Uddin, PhD

EQuIP CORNER

2026 AAHRPP REACCREDITATION SITE VISIT PREPARATION: WHAT SHOULD I KNOW?

McLaren is preparing for its 2026 AAHRPP reaccreditation site visit, expected this spring or summer. AAHRPP, the Association for the Accreditation of Human Research Protection Programs, sets the national standard for high quality human research protections. McLaren first earned accreditation in 2013 and has maintained continuous full accreditation through two successful reaccreditation cycles.

We have submitted our Step 1 Application to AAHRPP, which includes an overview of our Human Research Protections Program (HRPP), policies, IRB operations, and Education and Quality Improvement Program (EQuIP) materials. AAHRPP will review these documents and then schedule the site visit.

During the visit, AAHRPP representatives will conduct confidential interviews and review records to confirm that our policies and procedures are consistently implemented across the system. Anyone involved in human research could be selected for an interview, including investigators, coordinators, pharmacists and other research staff. Interview questions typically focus on regulatory and ethical responsibilities related to human participant protections.

Additional guidance and training will be provided as the visit approaches, but the following overview highlights what to expect.

Preparing for the Site Visit

A strong foundation begins with understanding the McLaren HRPP mission:

- Protect the rights, safety, and welfare of individuals who participate in research
- Support excellence in human subjects research

To uphold this mission, the McLaren HRPP follows all federal regulations governing human subjects research and maintains policies and procedures that promote ethical conduct while minimizing administrative burden.

If selected for an interview, respond directly to the question asked. If a question does not apply to your type of research, simply explain that. For example, a behavioral health researcher may clarify that FDA regulations do not apply to their work.

You should be prepared to discuss:

- Your role in protecting research participants
- Where to find McLaren HRPP Policies and Procedures
- How to report non compliance and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)
- The ethical principles and purpose of your research
- Regulatory standards that apply to your studies
- IRB submission processes in iRIS
- Your required training (CITI, GCP, etc.)
- Ethical and equitable recruitment practices

Roles and Responsibilities of Investigators and Research Staff

Investigators and study teams hold primary responsibility for protecting human participants. This includes understanding and applying the ethical principles outlined in:

The Belmont Report

- **Respect for Persons:** Participants are autonomous and must be provided with adequate information to make voluntary decisions. Informed consent is an ongoing process, not a single form or event.
- **Beneficence:** Maximize benefits and minimize risks.
- **Justice:** Ensure fair selection of participants and equitable distribution of risks and benefits.

Related McLaren policies include MHC_RP0115 (Informed Consent) and MHC_RP0116 (Vulnerable Subjects in Research).

Federal Regulations

- The Common Rule (45 CFR 46)
- 21 CFR 50 and 21 CFR 56 for FDA regulated research
- Additional federal and state requirements, including HIPAA

Be ready to describe how your team minimizes risks, monitors participants, and ensures equitable recruitment.

Investigator Compliance with IRB Requirements

Investigators and research staff must ensure that all research is conducted in compliance with McLaren HRPP policies and applicable regulations. Key responsibilities include:

- Obtaining IRB approval before beginning any human subjects research
- Complying with IRB decisions and requirements
- Submitting continuing reviews timely
- Securing IRB approval before implementing any changes to approved protocols or consent forms
- Reporting UPIRSOs, adverse events, and protocol deviations according to policy

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Protecting research participants is a shared responsibility across investigators, research staff, the McLaren IRB, external IRBs, institutional leadership, and federal oversight agencies. You are not expected to memorize every regulation, but you should know where to find information and be able to describe how you uphold participant protections in your daily work.

RESEARCH AROUND McLAREN

KARMANOS PHYSICIAN-SCIENTIST LED CLINICAL TRIAL STUDIES

PRECEDING FDA-APPROVAL OF NEW TARGETED INHIBITOR FOR AML PATIENTS

A new drug has received U.S. Food and Drug Administration (FDA) approval, in which the Barbara Ann Karmanos Cancer Institute played a crucial role. The oral targeted menin inhibitor ziftomenib (known by its brand name Komzifti™) received FDA approval on Nov. 13, 2025. Ziftomenib is a once-daily oral targeted therapy for adult patients with nucleophosimin 1 (NPM1)-mutated acute myeloid leukemia (AML).

Suresh Balasubramanian, MD

"AML is an aggressive blood and bone marrow cancer, and mutations in the NPM1 gene are among the most common genetic drivers of the disease in adult patients," explained Suresh Balasubramanian, M.D., hematologist and medical oncologist, member of the Hematology Oncology Multidisciplinary Team and the Molecular Therapeutics Research Program at Karmanos. "Ziftomenib blocks the menin–KMT2A/NPM1 pathway, which leukemia cells rely on for survival, making it a highly precise treatment option for this molecular subtype."

This therapy benefits patients with relapsed or refractory NPM1-mutated AML. Prior to this FDA approval, treatment options for these patients were extremely limited, with allogeneic stem cell transplantation being the only potentially curative choice–an option many patients could not pursue because of age, comorbidities or other contraindications. In addition, conventional therapy is often insufficient to treat the disease at this stage, but ziftomenib provides mutation-directed, targeted treatment.

"This approval represents a major milestone for patients with NPM1-mutated AML. For decades, AML treatment relied heavily on cytotoxic chemotherapy," said Dr. Balasubramanian.

NPM1 mutations are the most common in AML, accounting for approximately 30% of cases, according to a press release from Kura Oncology, Inc., the company that developed Komzifti. Twenty percent of those patients' cancers may not respond to first-line therapy, and 70% of those patients' cancers may relapse within 12 months to three years. For a disease that has very few effective treatment options, ziftomenib makes receiving therapy easier for patients. No longer having to do chemotherapy, patients will take one pill once a day.

"This approval represents a major milestone for patients with NPM1-mutated AML. For decades, AML treatment relied heavily on cytotoxic chemotherapy."

– Suresh Balasubramanian, MD

Dr. Balasubramanian was the principal investigator at Karmanos for three clinical trial studies of this new therapy, which led to FDA approval. This includes the phase I clinical trial study, "Ziftomenib in Relapsed or Refractory NPM1-Mutated AML" (published in the Journal of Clinical Oncology), where the drug was first investigated in humans, and the dosage of the drug was tested. Dr. Balasubramanian's team continued patient studies, offering a phase II trial. Results from studies demonstrated a deep response. Now, Karmanos offers phase III combination clinical trials using this treatment.

"We continue to enroll and treat patients in multiple ongoing studies evaluating ziftomenib in various treatment settings and combinations, in addition to now being able to prescribe the FDA-approved therapy," he described. "My research laboratory also conducted preclinical mechanistic and combination studies with ziftomenib even before the clinical trials started, and we continue to explore new scientific questions related to menin inhibition."

As Dr. Balasubramanian described, this new targeted approach to treating NPM1-mutated AML represents a continued paradigm shift toward precision therapies tailored to the genetics of leukemia.

"Ziftomenib adds an important new tool that has the potential to improve outcomes and expand treatment options for patients who previously had very limited therapies. We are proud that Karmanos played a meaningful role in bringing this therapy from early development to FDA approval," Dr. Balasubramanian said.

2026 AAHRPP REACCREDITATION

CONTINUED FROM PAGE 15

More information about the HRPP is available at **mclaren.org/main/research-integrity**. Updated policies and a revised HRPP Manual will be posted on this webpage soon as part of our ongoing improvements to the site.

AAHRPP may ask questions such as:

- How do you notify the IRB about proposed changes?
- What would you do if research data were lost?
- How do you report a participant complaint?
- What is an Unanticipated Problem, and how would you report it?

In Summary

Protecting research participants is a shared responsibility across investigators, research staff, the McLaren IRB, external IRBs, institutional leadership, and federal oversight agencies. You are not expected to memorize every regulation, but you should know where to find information and be able to describe how you uphold participant protections in your daily work.

AAHRPP interviews are intended to confirm good practices, not to test or intimidate. Preparation simply helps you feel confident and ready.

The McLaren HRPP team is here to support you throughout the reaccreditation process. If you have questions or would like assistance, contact us at **hrpp@mclaren.org**.

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

ARTIFICIAL INTELLIGENCE (AI) AND SCHOLARLY ACTIVITY

By Carlos F. Rios-Bedoya, ScD, MPH

Carlos F. Rios-Bedoya, ScD

Artificial Intelligence (AI) relies on large language model (LLM) algorithms that must be trained on extensive datasets. The more data these models receive, the better their performance becomes. However, they remain prone to errors, often referred to as "hallucinations," especially when dealing with highly specialized topics. Scholarly activity projects fall into this category. For this reason, results generated by AI tools require careful auditing and quality control to identify inaccuracies or misleading information. At this stage of AI development, we recommend that AI be used only by subject matter experts who can determine whether the output is accurate and reliable.

The McLaren Health Care (MHC) Scholarly Inquiry Division currently evaluates AI usage in all documents that disseminate scholarly activity results outside MHC. Our evaluation process includes three components. First, we review the document's formatting. Over time, we have become familiar with the default structure commonly produced by ChatGPT and similar tools. Second, as subject matter experts, we assess the accuracy of scholarly activity documents, including study design, sample selection, inclusion and exclusion criteria, assessments, and statistical analyses. We have observed that AI tools often attempt to include too much information from multiple domains, which can lead to impractical study designs, unrealistic sample sizes, and an excessive number of statistical tests, some of which may be incorrect. Finally, we use three top ranked AI detection tools to estimate the percentage of text that may have been generated by AI. In a recent evaluation, these tools identified AI generated content ranging from 96 percent to 99 percent. As a comparison, an original peer reviewed article I authored was scanned using the same tools, and all returned a result of 100 percent human produced content.

When high levels of AI generated content are identified in a resident or fellow's scholarly activity document, we address the matter politely and professionally with the individual. We encourage them to rewrite the material in their own words to ensure originality and accuracy. A formal policy on AI use in scholarly activity projects will be developed in the near future. For now, we recommend avoiding AI use, or at least minimizing it, in this context.

The Division of Scholarly Inquiry remains committed to supporting and facilitating scholarly activity for McLaren residents, fellows, and faculty. For additional information, please contact Dr. Carlos F. Ríos Bedoya at **carlos.rios@mclaren.org**.

UPCOMING RESEARCH EDUCATION

MHC Research Integrity Brown Bag session
Research Clinic
February 26, 2026

Speaker:
Susmita Jain

To register please email
Susmita.jain@mclaren.org

AAHRPP

2026 AAHRPP Annual Conference
Great Lakes, Great Minds Meet in Michigan
May 19-21, 2026
Detroit Marriott at the Renaissance Center, Detroit, MI

Scan the QR Code for more information and to register.

AAHRPP
Webinar: Why HRPPs Matter
February 17, 2026 | 1 p.m. - 2:30 p.m.

Presenters:
Debra Dykhuis
University of Minnesota
Rachel Karlnoski
University of South Florida Health and Tampa General Hospital
Scott Lipkin
Baptist Health South Florida

Scan the QR Code for more information and to register.

ACRP – NY Metro Chapter
Clinical Trials in the Age of Weight Loss Drugs
February 24, 2026 | 6 p.m. - 7:30 p.m.

Speaker:
Melanie Jay, MD, MS

Scan the QR Code for more information and to register.

ACRP
Responsible, Human-Centered AI: The Future of Clinical Research Roles
February 25, 2026 | 12 p.m. - 1 p.m.

Speakers:
Noelle Gaskill, MBA, ACRP-CP
Jennifer Sheller, ACRP-CP

Scan the QR Code for more information and to register.

ACRP 2026
April 24, 2026 | 12 a.m.
thru April 27, 2026 | 11:59 p.m.
Hyatt Regency Orlando 9801 International Drive, Orlando, FL

Scan the QR Code for more information and to register.

PRIM&R
Flash Learn: Research or QI? Strategies for DNP Projects
February 3, 2026 | 1 p.m. - 1:45 p.m.

Speakers:
Kelly Beiswanger, BA
Julie Zadinsksy, Ph.D., MS, BSN, CIP

Scan the QR Code for more information and to register.

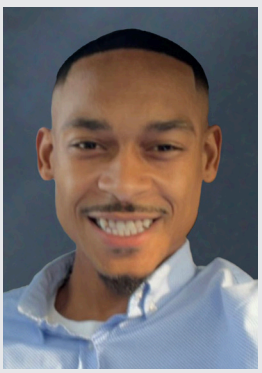
PRIM&R
Webinar: Who's Managing What? Understanding COI Oversight Within the HRPP
February 17, 2026 | 1 p.m. - 2 p.m.

Speakers:
Michael Hill
Deb Paxton

Scan the QR Code for more information and to register.

PRIM&R
Workshop: The Assurance of Privacy and Confidentiality in Research: Is it Still Possible?
February 26, 2026 | 1 p.m. - 2:30 p.m.

Scan the QR Code for more information and to register.



MCRI is pleased to welcome **Marcus Johnson** as a clinical research coordinator at the McLaren Flint location. Marcus, a Flint native and University of Michigan graduate, brings hands-on experience supporting and managing clinical trials across multiple therapeutic areas. He is also a Gates Scholarship recipient, an honor awarded to exceptional students with demonstrated academic promise. Marcus values supporting participants throughout their trial experience and looks forward to strengthening his expertise while contributing to study quality, patient outcomes, and overall research efficiency at MCRI.

THIRD ANNUAL

McLAREN HEALTH CARE

SCHOLARLY INQUIRY FORUM

Friday, April 24, 2026 – Somerset Inn, Troy

CALL FOR ABSTRACTS

GME Residents/Fellows/Faculty, Nursing Professions, and Other Clinical Professions are invited to submit completed abstracts to be considered for oral presentation, e-poster presentation, or poster showcase acceptance at the Third Annual MHC Scholarly Inquiry Forum.

Medical students are invited to submit completed abstracts to be considered for the poster showcase only, given McLaren Resident(s)/Fellow(s)/Faculty have been involved.

There are three possible categories for submission:

1. **Quality Improvement:** systematic, data-driven initiatives to enhance health care by standardizing processes, reducing variation, and improving patient outcomes, often involving developing new practices, testing changes, and analyzing results to achieve measurable, sustainable improvements in patient care and system efficiency.
2. **Research:** systematic, evidence-based investigations designed to generate new knowledge, test hypotheses, or evaluate existing practices through structured methodology, data collection, and analysis.
3. **Case Reports:** a detailed narrative that follows the structured CARE Guidelines to accurately and transparently report a patient's case.

IMPORTANT DATES

- **February 15, 2026**
  Abstract submission deadline
- **March 2-15, 2026**
  Abstract review period
- **Week of March 23, 2026**
  Abstract acceptance notices
- **March 31, 2026**
  Event registration deadline
  Oral Presenters, E-Poster Presenters, and Poster Showcase Participants must register within one week of notice or risk disqualification and are expected to attend the full day of events.
- **Week of April 6, 2026**
  Presentation schedules released to participants/judges
- **April 13, 2026**
  Copies of accepted oral presentations and e-posters due

McLaren

For more information, email **scholarlyinquiryforum@mclaren.org** or visit the event website.

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We sincerely regret if we left out any fellow or resident, due to our publication deadline. Nevertheless, our congratulations to all of you that received any recognition for your scholarly activity work. We also would like to recognize faculty, program directors, and all medical education staff for their support and assistance. Without you, none of this would have been possible.