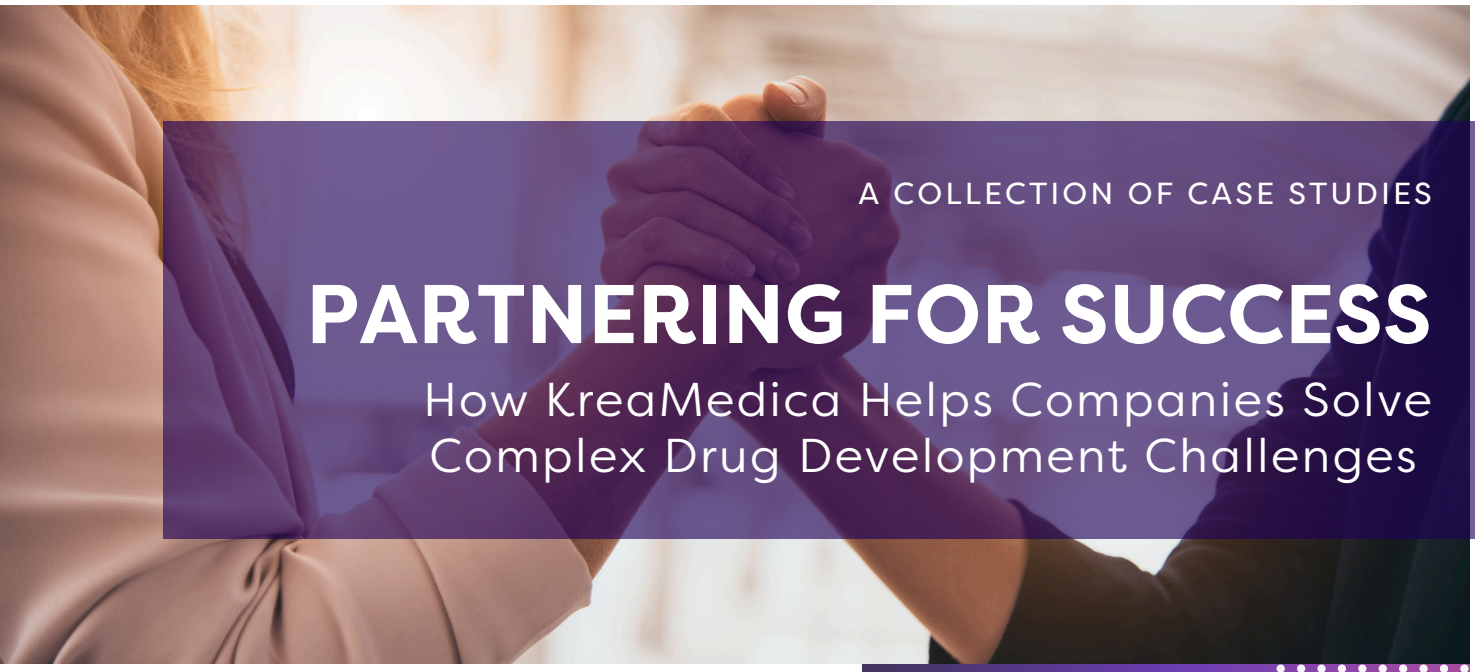
KreaMedica



A COLLECTION OF CASE STUDIES

PARTNERING FOR SUCCESS

How KreaMedica Helps Companies Solve Complex Drug Development Challenges

Drug development journeys inevitably encounter roadblocks—but not all companies navigate them the same way. The difference between success and costly delays comes down to having the right expertise when challenges emerge. At KreaMedica, we work alongside biotech and pharma innovators throughout the development lifecycle. We recognize that every program is unique—and so is every solution we provide.

As your one-stop drug development partner, we help identify the right vendors and experts, manage budgets and timelines, and provide hands-on oversight from planning through execution. Our experienced team meets clients where they are, offering scientific insight, project management and the continuity needed to overcome even the most complex hurdles.

The three case studies that follow show how KreaMedica adapts to diverse client needs—from optimizing toxicology study design and streamlining bioanalytical assays to resolving critical issues in preclinical development.

I don't really know how we would have completed the project without KreaMedica under all the circumstances.

Tom Fritz, COO, Cairn Therapeutics

ABOUT KREAMEDICA

KreaMedica was founded in 2009 with a vision to revolutionize drug development through functional outsourcing. The Montreal-based company has planned, managed and executed over 150 development programs from lead candidate selection through non-clinical safety assessments and early clinical trials by outsourcing to their world-class CRO/CMO network. With a commitment to research, development and quality, KreaMedica has become a trusted “one-stop shop” drug development partner, offering reliable solutions and cost-saving strategies for their international biotech and pharma clients.

KreaMedica

A COST-EFFECTIVE, REMOTE TOXICOLOGY SOLUTION FOR CAIRN THERAPEUTICS

Cairn Therapeutics is a pharmaceutical company with a mission to help beat cancer. Its team is developing a novel drug for solid tumours and possibly blood-borne cancers that has the potential to revolutionize chemotherapeutic treatments.

The first-in-class DNA binding agent, CT-262, was developed by renowned chemist Dale Boger, Ph.D, a premier researcher on duocarmycin drugs at Scripps Research. CT-262 is a pro-drug that is converted into an active form inside cells. It is a promising breakthrough high-potency cancer treatment with a reduced impact on the immune system and long-lasting action.

"The pre-clinical data on the efficacy of this drug was pretty substantial, with the potential to replace a significant portion of the current chemotherapeutics that are on the market," said Tom Fritz, COO at Cairn Therapeutics, "It would be a shame if this drug was not tested clinically for its true potential in treating human cancers."

KreaMedica assisted Cairn Therapeutics in preparing the Investigational New Drug (IND) application package for their lead candidate, CT-262. We asked Tom Fritz to share some of the challenges that KreaMedica helped their team overcome.

When Tom Fritz joined Cairn Therapeutics as COO, he was well-equipped to guide the drug development and regulatory submission process, with 30 years of experience and the successful completion of numerous major clinical trials. However, no two drugs are the same, and getting CT-262 ready for IND submission came with a set of unexpected challenges.

Challenge #1: Finding the right CRO and overseeing toxicology studies in Canada

Conducting non-clinical toxicology studies in the U.S. comes at a substantial cost.

"We were seeking a more budgetary-friendly option," said Tom. Cairn Therapeutics discovered a toxicology research lab in Montreal that offered substantial cost savings. However, because the safety studies were taking place during the COVID-19 pandemic, their ability to travel to the site was limited. KreaMedica became an intermediary between Cairn Therapeutics and the toxicology CRO, helping with the development of study plans, on-site monitoring, guidance and review of reports.

"They quickly assigned a program manager and a scientist with substantial toxicology background and a good understanding of the regulatory requirements," added Tom. "They were both very competent and did a remarkable job."

Thanks to KreaMedica's on-site monitoring, Cairn Therapeutics was able to establish if side effects were due to technical difficulties or the drug itself. Additionally, working with a Canadian service provider through KreaMedica provided a favourable cost structure due to the Canadian Scientific Research and Experimental Development (SR&ED) tax incentives, which resulted in substantial cost savings for Cairn Therapeutics.

"Thanks to KreaMedica, we were able to execute our toxicology studies on a smaller budget and nimbly in a foreign country, especially when travel was restricted due to the pandemic," said Tom.

Challenge #2: Establishing the right dosing schedule and thresholds

CT-262 is a pro-drug molecule that goes through a two-step enzymatic activation mechanism in the hypoxic tumour microenvironment, remaining mostly in its inactive form in healthy cells. This drug has a substantial half-life, so once it gets into the cells, it will maintain cytotoxic effects for a fair amount of time. While this provides a significant benefit in terms of the drug's potency, establishing the maximum tolerable dose presented challenges around the dosing schedule and thresholds.

KreaMedica helped Cairn Therapeutics interface with the toxicology labs to develop the appropriate study protocols and resolve issues that arose due to the drug's high potency. Through on-site monitoring and in-person discussions with the study director, KreaMedica was able to provide an accurate and objective picture of the status of the studies and work with the obstacles of the product, such as the dosing schedule and formulation.

> **KreaMedica was instrumental in managing the preparation of the study reports, as well as editing and support. When we got the report, it had been substantially refined and cleaned up, which helped to expedite the process.**
>
> *Tom Fritz, COO, Cairn Therapeutics*

Challenge #3: Preparing reports for IND submission

In addition to managing the toxicology studies, KreaMedica helped define the requirements of the IND submission package based on Cairn Therapeutics' molecule and indication, removing studies and methods that were not required for their situation (such as dose formulation analysis).

"They were instrumental in managing the preparation of the study reports, as well as editing and support," said Tom. "When we got the report, it had been substantially refined and cleaned up, which helped to expedite the process."

"KreaMedica's assistance in regards to the quality of the data and the reports will most certainly facilitate the [IND submission] and favourable review," said Tom.

Challenge #4: Project development plan for bridge funding

Since completing the IND submission package, Cairn Therapeutics has reached out to KreaMedica for help on a different project. Cairn Therapeutics is developing a next-generation product and soliciting bridging funding during the development cycle. KreaMedica provided expertise in designing the study program for the new generation drug and putting forward a budget with sufficient details to inform investors.

Despite initial challenges, including formulation issues and toxicity concerns, the team overcame these hurdles with KreaMedica's help, which provided cost-effective program management and toxicology expertise. The drug is now ready for IND submission, with the potential to revolutionize chemotherapy treatments by offering greater efficacy and safety.

"I don't really know how we would have completed the project without KreaMedica under all the circumstances," said Tom, summing up the interaction between Cairn Therapeutics and KreaMedica.

KNOWING WHEN TO LET GO OF A PROJECT: A CASE STUDY WITH ADAMED PHARMA

Adamed Pharma is a leading pharmaceutical and biotechnology company, with over 900 products and 256 patents covering 19 therapeutic areas. It was the first Polish company to undertake research into innovative therapies back in 2001. Adamed had significant experience with internal R&D and had built strong early-stage scientific capabilities. But as it moved toward development, it faced a challenge familiar to many biotechs: translating promising molecules into viable drug candidates.

To bridge this gap, Adamed turned to KreaMedica in 2011 for expertise in real-world drug development. Marcin Kolaczkowski, who led Adamed's central nervous system (CNS) projects team, worked closely with Karl-Rudolf Erlemann (Rudi), President & CEO of KreaMedica. The collaboration, which lasted nearly a decade, proved to be remarkably fruitful. We asked Marcin to share more about his experience working with KreaMedica.

Challenge 1: Bridging the knowledge gap between drug discovery & drug development

Adamed's team had deep expertise in CNS pharmacology and medicinal chemistry. They were able to formulate strong hypotheses, propose methodology and execute drug discovery studies, which resulted in several promising drug candidates. However, drug development—especially in the preclinical space—was uncharted territory.

"We had quite a bit of experience at the drug discovery stage and clinical assets in diabetes, but we had never developed molecules in the CNS area before," said Marcin. "So we reached out to KreaMedica to help us develop our preclinical capabilities."

KreaMedica's founder, Rudi, brought the drug development expertise and real-world context, with a focus on developability—an essential element for translating discovery-stage hypotheses into viable clinical candidates.

This experience later helped Marcin develop a new Drug Discovery and Development Master's program at the Jagiellonian University Medical College. The program focuses on the practical side of drug discovery and development, particularly early preclinical development, such as profiling of molecules, selection of drug candidates and development.

"The challenges we tackled at Adamed with Rudi helped us offer the students something more than just textbook knowledge," said Marcin. "And much of that experience and knowledge came from our work with KreaMedica."

Challenge 2: Enabling "fail fast" decision-making

Adamed's scientific process was rigorous. Yet, like many discovery-stage teams, they faced a common trap: holding onto molecules with promising biological activity despite underlying issues, such as unfavourable pharmacokinetics or formulation. Through collaboration with KreaMedica, Adamed learned to embrace a "fail fast" mindset. Together, they evaluated and de-risked assets early, focusing on solubility, metabolic stability, oral absorption, selectivity and off-target profiling.

"We killed several molecules that looked promising at first—but just weren't developable. And we were glad we did," said Marcin. "Everything that is potentially problematic will bite you eventually. The sooner you find out, the better."

By applying developability filters early in the pipeline, Adamed avoided costly late-stage failures and concentrated resources on their most promising asset—one that was ultimately commercialized with Acadia Pharmaceuticals, a U.S.-based company focused on developing breakthroughs in neuroscience, in 2021.

"What KreaMedica provided was the resolve to say, 'No, this is not going to work,' even when we were emotionally invested," Marcin said.

Challenge 3: Assembling and managing specialized service providers

Beyond development strategy, KreaMedica played a central role in organizing and managing the preclinical research service providers.

"In addition to his own knowledge and experience, Rudi always brought on board good people," said Marcin. "He assembled the right team of specialists for the challenges we faced. They brought the expertise and proficiency, and because the service providers were located in Canada, we were able to take advantage of Canadian tax credits. This business model proved really beneficial for us."

KreaMedica became an extension of the Adamed team, co-leading the projects with the contracted CROs, managing timelines and ensuring a seamless workflow from strategy to execution. This integrative model allowed Adamed to expand its research capabilities and efficiently move programs forward.

"They became part of our team. It was a real knowledge transfer, not just outsourced work, which allowed us to build experience ourselves."

Project Outcome

One of the greatest benefits of working with KreaMedica, according to Marcin, was the ability to identify the weak points in projects and make better decisions about which compounds to take forward.

"KreaMedica helped us identify critical developability issues in several of our drug candidates and helped us make difficult choices that ultimately led to the right candidate selection," he said. "We had to 'kill' several molecules, and we were ultimately really happy to have KreaMedica's assistance in making those decisions."

With KreaMedica's guidance over a decade-long collaboration, Adamed advanced numerous small molecules and biologics, by making smarter go/no-go decisions and, ultimately, successfully brought a molecule to commercialization.

This experience and knowledge became the foundation of the Master's program that Marcin started, training the next generation of scientists to understand both the science and strategy needed to succeed in biotech.

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Marcin Kołaczkowski, Lead CNS Scientist, Adamed Pharma

KreaMedica

BUILDING LASTING PARTNERSHIPS: A CASE STUDY WITH RK WOLFF SAFETY CONSULTING

Ron Wolff, president of **RK Wolff Safety Consulting Inc**. and former Vice President of Regulatory Affairs & Toxicology at Pulmokine, is a long-time collaborator of KreaMedica. He has been working with KreaMedica since its inception and has come to know Karl-Rudolf Erlemann (Rudi) and his team as trusted partners in supporting his client's programs. Before starting his own consulting business, Ron had worked as a former Executive Director of preclinical safety assessment for Novartis, as well as at Nektar Therapeutics, Eli Lilly and the Lovelace Inhalation Toxicology Research Institute.

As a seasoned expert in preclinical safety assessment and toxicology, with a particular focus on inhalation toxicology and pharmaceutical aerosols, Ron has contributed his knowledge to many joint projects with KreaMedica over the years. This long-standing partnership has supported successful outcomes for many clients. "KreaMedica has been instrumental in navigating several challenges that have occurred with the different projects," said Ron.

In an interview, he described the extensive interactions he has had with the KreaMedica team, highlighting how their deep expertise and coordinated problem solving helped resolve complex toxicology challenges and advance several compounds towards commercialization.

Challenge 1: Designing a complex toxicology study with multiple active ingredients

Ron and KreaMedica worked together to help an early-stage biotechnology company in the respiratory disease space get a successful IND application for one of their lead candidates. But like most IND submissions, this one was not without challenges.

The test agent in this project contained a combination of three active ingredients, requiring a toxicology study that could easily become unwieldy in scope and cost. Based on the initial assessment, the study design could require over ten different study groups—an extremely time-consuming and costly undertaking. "The study design was one of the most complicated I have done," said Ron.

In the end, the joint effort and expertise allowed to reduce the number of study groups down to eight. Ron expressed that KreaMedica was instrumental in developing and executing the successful study along with a Canadian CRO partner, ITR Laboratories Canada, located in Montreal, Quebec. The streamlined study design resulted in significant cost and time savings for the client without compromising data quality.

Challenge 2: Streamlining bioanalytical assays for multi-compound analysis

In addition to solving logistical challenges related to the study design, KreaMedica was also involved in helping facilitate bioanalytical work. The presence of three distinct compounds in the test formulation introduced complexity to bioanalytical methods. To avoid the need for separate analytical runs for each compound, the team designed an ingenious solution to dramatically reduce the number of runs.

"Rudi's bioanalytical expertise helped immensely in developing a streamlined assay, which allowed analysis of two of the compounds in one run," said Ron.

This approach, executed with the help of a Quebec-based company Royalmount Laboratories, not only helped reduce the time and cost of the analytical work, but also decreased the variability between assays. The successful completion of these studies led to an IND submission, and the drug combination is now in clinical trials.

Challenge 3: Diagnosing & resolving unexpected toxicities in chronic inhalation studies

KreaMedica and Ron also collaborated on a different small molecule project for a clinical-stage biopharmaceutical company. After successful one-month toxicology studies, the 6- and 9-month

> **KreaMedica provided a much more extensive monitoring of the studies carried out by the CRO than is usually possible for a sponsor. KreaMedica's team members are intimately familiar with the labs. They provide thorough project management and study monitoring, along with excellent insights.**
>
> *Ron Wolff, President, RW Wolff Consulting Inc.*

chronic studies revealed unexpected toxicities, threatening the program's continuation. KreaMedica's team led an in-depth investigation and uncovered a key issue: a modification to the aerosol generation system had been introduced after the one-month studies.

"KreaMedica provided a much more extensive monitoring of the studies carried out by the CRO than is usually possible for a sponsor," said Ron. This deep level of engagement and oversight was what helped identify the problem with the aerosol generation system. "KreaMedica's team members are intimately familiar with the labs. They provide thorough and frequent project management and study monitoring, along with excellent insights."

By identifying and correcting the system change, the team was able to restart the studies, salvaging a program that would otherwise have been abandoned. The studies are now supporting Phase 2 trials and potentially a New Drug Application (NDA) submission.

Facilitating collaboration and reducing development costs

The projects that Ron described involved many stakeholders with unique needs and constraints. In each case, KreaMedica played a crucial role as a cross-functional integrator, providing scientific oversight, project management and troubleshooting across multiple engagements. This continuity and strategic input ensured smooth execution of projects and enabled all parties—consultants, CROs, bioanalytical labs and sponsors—to work cohesively under a unified development plan.

"These services are invaluable," expressed Ron. "KreaMedica helps with study designs, sending out RFPs to CROs to get the best possible prices for studies. The pricing for sponsors is considerably reduced when the studies are conducted in Canada under KreaMedica's close oversight, adding up to substantial cost savings."

By working with Canadian CROs, KreaMedica provides tangible financial benefits for its clients: a sponsor gets a reduced price for the study in addition to enhanced monitoring, thanks to KreaMedica's proximity to the CROs. This eliminates the need for frequent trips to a remote site for the client and allows them to focus their efforts on other projects. KreaMedica also provides crucial supervision of the studies, reports and project management services to keep things on track.

"The fact that KreaMedica is in close proximity to several key toxicology labs means that they can provide much more extensive monitoring than is usually possible for a sponsor," said Ron. "They are highly knowledgeable and easy to work with."

THE POWER OF PARTNERSHIP

As these case studies demonstrate, the most daunting obstacles become turning points with the right support. Complex drug development challenges require collaborators who can anticipate problems before they derail programs, act decisively when time is critical, and pivot quickly as circumstances change.

At KreaMedica, we've built our approach around delivering exactly this kind of partnership. We bring together scientific expertise, hands-on project management and industry relationships that matter when programs face critical junctures. Whether you're navigating regulatory complexities, need specialized insights or want to optimize your development strategy, we're here to help you move forward.

Ready to advance your program?

Contact us to discuss how we can help you achieve your development goals and connect you with partners who understand what it takes to bring therapies to market.

KreaMedica