

Case Study

Metabolic Modulators Research Ltd.

Introduction

Commercializing the results of medical research always seemed like a good idea to Dr. Gary Lopaschuk. For someone else, that is. The University of Alberta professor of Pediatrics and heart researcher never regarded commercialization as something he would take on.

Not that Lopaschuk hasn't worked with industry. In fact, his research on heart metabolism has garnered a great deal of industrial interest. Pharmaceutical companies routinely approach Lopaschuk's Cardiovascular Research Group to determine how their metabolic agents act.

But about four years ago, Lopaschuk started to look beyond contracts with industry. He began to wonder whether it might be possible for his group to independently develop compounds that could be used as drugs to reduce tissue damage during heart attacks. He set up a company, Metabolic Modulators Research Ltd. (MMRL), and began an in-house heart drug development program. This work was funded by revenue from the contract work, strong support from the University of Alberta for facilities and legal costs, an IRAP grant from the National Research Council, and TC funding from the Alberta Heritage Foundation for Medical Research.

By June 2000 the company was fast approaching a crossroads. Where will MMRL find the money to continue its in-house drug development program? Should the contract area be allowed to expand to generate more revenue? Who would direct the increasingly complex business activities of the company?

These are just some of the questions Gary Lopaschuk pondered in the early summer of 2000. There were personal issues as well. More and more of his time was being taken away from his basic and contract research to deal with issues that were not within his realm of expertise. As MMRL moved products closer to commercialization, business expertise would become even more necessary. How would Lopaschuk's role in his company evolve? He wanted to continue his basic research and had to be sure there was no conflict between this and MMRL's activities.

A look at the science

The classic approach to treating a heart attack involves interventions aimed at increasing oxygen supply to the heart muscle or decreasing the oxygen demand of the muscle. Lopaschuk has pioneered a new approach to treating heart attacks by improving the efficiency of oxygen utilization by the tissue.

Normally, the heart muscle uses a balance of fatty acids and glucose for fuel. But during and immediately after a heart attack, high levels of circulating fatty acids effectively compete with glucose as a source of energy. This results in tissue damage in the heart muscle.

Lopaschuk's research has identified a number of enzymes that induce this unhealthy shift in metabolism. These are "target enzymes". The new approach involves finding compounds that inhibit the action of these enzymes, thus limiting fatty acid oxidation and increasing glucose oxidation. The drug shifts the heart back to more optimal fuel use.

A look at the company

MMRL was incorporated in 1998.

Vision: To enhance the life and well being of people through preemptive science and non-intrusive treatment in cardiovascular disease.

Mission: To position its life sciences strengths in heart drug research to become a profitable global technology provider, through collaborative partnerships with industry in heart drug development.

The company now has 15 employees.

Management personnel are:

- President and CEO Gary Lopaschuk, PhD, directs operation of all scientific affairs and provides direction for business operations.
- Vice President, Scientific Affairs, Jason Dyck, PhD, leads the process and monitoring controls. The scientific team reports to Dyck.
- Vice President, Business Affairs, Frank Borsato oversees business operations and business negotiations and transactions.

MMRL currently generates revenue primarily from contracts for testing services from pharmaceutical and biotechnology companies. The work involves compound screening and efficacy testing in an intact working heart model.

This revenue supports research and drug development. These areas also receive support from:

- Alberta Heritage Foundation for Medical Research (AHFMR) Technology Commercialization program. Phase 2 funding for the screening of lead compounds and related equipment and personnel.
- National Research Council (NRC). Subsidization of a six-month scientific position

- University of Alberta provides the leased facilities and contributes toward the costs of patent applications, filing and litigation.

The link to research

Since completing his PhD in 1983, Lopaschuk's research has been devoted to the study of energy metabolism. At the outset of his career, he was one of only a handful of scientists in this area. But within the last five years, interest in energy metabolism has grown within the scientific community. For example, a March 2000 editorial in the journal *Circulation Research* outlined the potential of metabolic therapies for heart disease and called for further research.

Lopaschuk continues fundamental research on energy metabolism aimed at elucidating basic questions such as: Why does abnormal energy metabolism contribute to heart disease? How is energy metabolism regulated?

This research is the foundation of MMRL. It is the source of new target enzymes and the reason Lopaschuk's lab has developed expertise that is sought worldwide. MMRL's core capabilities in contract research and drug development are based on this world-class fundamental research.

Contracts

MMRL's laboratory is equipped with the state-of-the-art equipment and tools necessary for this research; his R&D team has years of expertise in the area. As a result, Lopaschuk and his lab are in great demand especially by pharmaceutical companies, which generally do not have in-house expertise in energy metabolism.

When MMRL was formed, contract activity was moved inside the company and is a source of revenue. MMRL has key contracts with three pharmaceutical companies which involve working on a specific target enzyme. The companies have an exclusivity agreement with MMRL concerning the targets.

Lopaschuk says there are about four other companies that are keenly interested in having MMRL do contract research for them. But he is reluctant to enter into many more contracts. Although they provide a stable source of revenue, contracts take time and manpower away from in-house drug development activities.

Drug development

Even before MMRL was officially set up, it had a long-term deal with a pharmaceutical company to explore one particular target enzyme.

However Lopaschuk wasn't entirely satisfied. "This deal concerned only one enzyme and we knew of others to target. The idea of giving them all away so soon didn't sit well," he

says. “So we talked about doing more of the work on our own before taking on a partner.”

It was clear that if MMRL was to do this, the company would need extra resources and advice, as well as expertise in medicinal chemistry. Resources and advice have come from AHFMR’s Technology Commercialization Program, NRC’s Industrial Research Assistance Program (IRAP), and the University of Alberta’s Industry Liaison Office. The expertise comes from University of Alberta chemistry professor Dr. John Vederas, who has a collaborative agreement with MMRL.

The R&D was successful. MMRL identified a lead compound for the treatment of angina and angina pectoris. While research continues, the focus on the business side is developing marketing and business plans. Lopaschuk is determined to try to advance the technology as far as possible. How far will – and can – MMRL go with in-house development?

A look ahead

The next step for MMRL’s lead compound is pre-clinical animal testing, which is comprised of toxicology, pharmacokinetics and in-vivo efficacy testing.

“The animal testing is important because a compound can appear promising in the lab but if it’s toxic or only exists in the body for a few minutes, then it’s no good as a drug,” Lopaschuk says. “I’m hoping we can go as far as getting Investigational New Drug approval for the compound. I think development beyond that would be impractical for us.

“The advantage of doing this independently is that we will get higher royalties and attract more interest from companies. It’s the difference between a concept and a potentially viable compound.”

The intent is to outsource the pre-clinical work to contract research organizations. MMRL estimates that this work will take two years and cost approximately \$700,000.

MMRL intends to make an application to the AHFMR’s TC program for Phase 3 funding of \$500,000. If this application is successful, the funding will cover a substantial part – but not all – of the pre-clinical work on the lead compound.

MMRL has potential to develop more drugs than this one compound. At the moment, the company has four or five target enzymes to explore. And as the main thrust of Lopaschuk’s research is to understand the mechanics of these heart enzymes, new targets will likely be found.

“I think we have a three-year window to develop new compounds,” he says. “It’s only a matter of time before the big pharmaceutical companies duplicate our drug development process. What we’ve done with MMRL is create a way for us to capitalize on our lead

and get more value out of the research here in Alberta. Without MMRL, we'd be selling our technology at an early stage out of the province, and most likely out of the country."

Unlike many small new ventures that are involved in drug research and development, MMRL has saleable patents and new chemical entities in its possession. This puts it in a somewhat enviable position, as it mitigates risk. However, it makes planning for the future more complex.

What's next for MMRL?

"We need to identify a business leader to take our company to the next stage," says Lopaschuk. "It isn't the scientific expertise we need, we need the business expertise to sort through the issues and options, develop a plan, and find the money to do it.

"I can sell the science, but I don't have the expertise to determine what is the best route for the company, nor do I have the time to spearhead this initiative. This is the point we're at."

Points to ponder

- What are the primary issues Lopaschuk has to address before developing a strategy?
- In developing a strategy where can Lopaschuk go for advice on financing and corporate organization?
- Lopaschuk has been very careful to keep confidential the details of both MMRL's contract research and its in-house drug development program. As the company seeks financing, he is wondering how to balance confidentiality with the need to disclose business activity.