



Turning the Cash-flow Corner

Having toiled for years in cash-burning obscurity, Alberta's leading biotech companies are poised to make the long-sought leap from straight research to marketing, manufacturing and the prospect of profitability. But do they have the tools and the talent to make the transition?

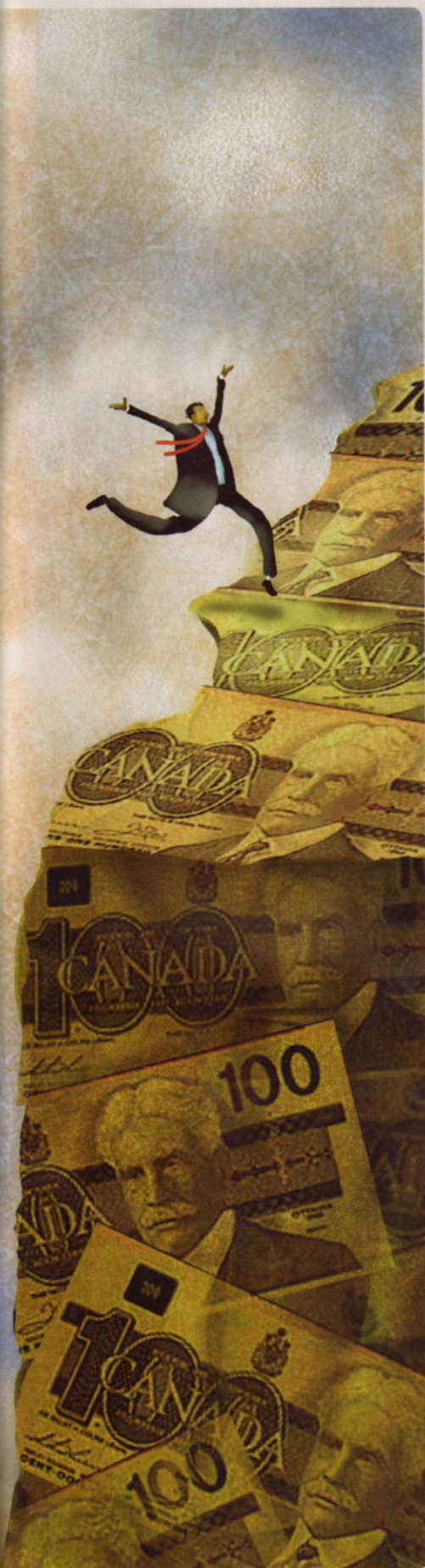
BY MARINA MICHAELIDES
ILLUSTRATION BY DAVID CUTLER

Marc Canton arrived in Edmonton in 2005 from Toronto, where he helped grow Biovail Corporation from 100 to 2,800 employees, including building a sales force from scratch. By the time he left, Biovail was posting annual sales approaching a billion dollars, with a 25% profit margin. His new job as president of ViRexx Medical Corporation, a University of Alberta offshoot set up to develop OvaRex, a vaccine for late-stage ovarian cancer, takes him back to square one.

Canton sees himself as the midwife in charge of a baby. Among his many challenges, he says, the hardest "is to change the mindset from academic research to marketing." So far, he has hired a management consultancy "to turn a group of people into a team" and three

specialists from out east to oversee licensing and drug trial regulation. But he has his work cut out to turn ViRexx into the next Biovail, itself an exception in the Canadian health sciences scene.

ViRexx is just one of a handful of biotechnology companies in Alberta that are approaching the magic moment of commercialization, when the technology they have spent years refining can be brought to market and sustained revenues finally flow in. Unfortunately it's not as easy as it sounds. Many Canadian biotechs have stumbled at this juncture, jeopardizing the patient investment of their backers



over years of controlled cash burn. Truth is, things like licensing, marketing and manufacturing require a whole different skill set from the things most Alberta biotechs have been doing to date: research, patenting and raising money. So what are these great biotech hopes doing to prepare for the transition? Will the scientists who have nurtured their babies through a long childhood love their kids enough to let them go?

Canada's health sciences sector as a whole resembles a high school full of gawky teenagers, not quite ready to support themselves. With 450 companies, Canada is second only to the United States in the number of biotech firms, but only 14 are profitable. According to accounting firm Ernst and Young's Global Biotechnology Report 2006, the Canadian share of global biotech product sales is 4% (\$13.7 billion US), compared to 77% (\$246 billion US) for the U.S. Alberta's toddler-share of the national sales pie is 3.5%, or \$386 million, according to the industry association BioAlberta.

Across the country there are "Too many, too small and too early-stage companies," concludes Ernst and Young. In Alberta, there are 106 bio-industry companies (including agriculture and environmental research firms), yet less than a third have a product on the market.

Compared to other provinces, "Alberta does not have access to as much VC [venture capital] funding," admits Michael Welsh, president of Edmonton-based Almasa Capital Inc. The province accounts for just 1.5% of the national VC biotech spend. Which is why Alberta's cash-starved fledgling companies are forced to "go public too early and then, typically end up undervalued," explains Mary Earle, an independent biotech consultant in Calgary. Alberta's 14 biotech IPOs account for 18% of the national total but have attracted only 11% of public investment in the sector. The average market capitalization is \$89 million, less than the cost of an average cancer drug trial. Biotech is not a business for the fainthearted.

To imagine what could happen next for Alberta's biotech sector, consider an example from next door in B.C. Today QLT Inc. has a widely prescribed drug on the market and a

STUCK IN THE LAB: A half-dozen companies are close to commercialization, though



"WHEN I CAME ON BOARD THE STRATEGY WAS NON-EXISTENT," SAYS SEMBIOSYS CEO ANDREW BAUM.

market cap of \$720 million. In the mid 1990s, QLT struggled on a shoestring, alone after losing its big pharma development partner, American Cynamid Company. To survive, the company focused on one product, funding its development by selling off all intellectual property rights to its other drugs. QLT found a new, bigger partner in Novartis AG. The plan worked. QLT's first drug, Visudyne, became the most successful ophthalmic drug-launch on record, selling \$150 million in its first year (2000).

Alberta's only such poster child for suc-

cessful commercialization is Edmonton's CV Technologies Inc. The company's lead product, Cold-fX, became Canada's top selling cold and flu remedy in 2005, with \$10.1 million profits on sales of \$31.9 million. Two years before, the company was on the brink of bankruptcy. Jacqueline Shan, a U of A pharmacologist and inventor of ChemBioPrint, the fX platform technology, took over the company as CEO. She made up for her lack of marketing experience by appointing those who had it: Norm Oliver, head of sales and marketing, and PR veteran Warren Mitchell, as vice-president,

communications. Cashless, the three designed the labels and branded fX products as preventative medicine rather than curative. An endorsement from the Edmonton Oilers and television personality Don Cherry (in exchange for stock options) made the front page of the *National Post* on September 24, 2003, and CV hasn't looked back.

Nonetheless, CV is viewed as an anomaly, operating in the over-the-counter "nutraceutical" niche as opposed to the highly regulated pharmaceutical sector. Like other biotechs, CV has spent millions (\$17 million so far) testing fX technology up to Phase II trials, the initial tests of toxicity and safety required to approve a drug. But CV has yet to negotiate the

minefield of "pivotal" Phase III trials that cost between \$30 million and \$100 million, the ultimate test to prove that a drug actually works on humans, and a necessary step for prescription medicine, which accounts for the bulk of the biotech revenue stream. It's the outcome of these results that Alberta's seven leading biotechs - CV Technologies, Biomira Inc., BioMS Medical Corporation, Isotechnika Inc., Oncolytics Biotech Inc., SemBioSys Genetics Inc. and ViRexx - are eagerly awaiting.

The crucial question of how to fund these pivotal trials ends up dictating the drug's marketing strategy. "For the first product at least, you need 'parents' [large pharmaceutical partners] to get to market, a company with a proven track record, because the costs of commercialization are so enormous," warns Karen Boodram, a stock analyst at Pacific International Securities. In exchange for an experienced partner's help, the junior partner gives up a share of sales of the final product.

To manoeuvre these complex deals with multinational drug marketers and still be left with a fair share of the proceeds takes skill and experienced managers. Michael Welsh warns, "Almasa invests in strong management. Scientists don't have the experience. So we try to dissuade them" from going it alone.

"Recruiting experienced management is the second-highest priority identified by biotech companies," according to the Canadian Life Sciences Industry Forecast 2006 from PricewaterhouseCoopers and national industry organization BioteCanada. In Alberta, "Staff is the No. 1 key issue," says Ryan Radke, president of BioAlberta. "Biotechs don't work without key people in business development to negotiate deals with big partners and experts in the regulatory environment. Drug trial approvals run into million-page documents." The province has a handful of managers whose experience has grown with the companies they founded. The rest, so far, have been imported.

Andrew Baum, seasoned from 16 years' experience at California-based Calgene Inc., was headhunted by founder Maurice Maloney to run Calgary's SemBioSys Genetics. A University of Calgary scientist, Maloney discovered how to grow insulin and other proteins in safflower plants, but knew little about growing businesses. In 1998, "Maurice pushed aggressively

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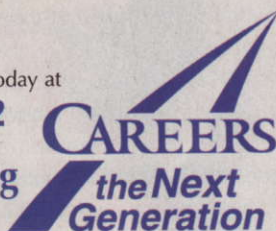


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to get someone with my experience – unusual for a scientist!” applauds Baum. “When I came on board the strategy was non-existent.” Since then, he has raised millions from his VC contacts, the stock market and licensing deals from agro-biotech products, and SymbioSys has enough cash to cover research and development until 2009, when the firm expects to release the results of human trials. Then he’ll look for a marketing partnership.

Fact is, few early-stage biotechs can even hope to market and manufacture a product on their own – as CV Technologies, improbably, did. Licensing deals are the main source of revenue to pay for a product’s development other than raising money on the markets. Getting the complex contracts right, therefore, is critical for successful commercialization. In ex-

QLT FOUNDER AND CHAIR JULIA LEVY DESCRIBES THE ART OF PRICING AS “NOT A VERY ADMIRABLE PROCESS. YOU CHARGE WHAT THE MARKET WILL BEAR.”

change for granting a third party the right to use, manufacture or distribute part or all of their technology, biotechs get cash. The deals include license fees to use a drug or procedure, upfront payments (akin to a signing bonus), milestone payments when pre-set scientific milestones or sales volumes are reached and royalties, a percentage of end-market sales. Considering that pharmaceutical industry profits are split roughly 30/70 between manufacturing and sales and marketing rights in various territories around the world, the contracts are a balancing act that weigh the financial risk of developing a drug against the potential profits to be made and the expertise each partner brings to the table.

Andrew Baum has a “holy trinity of value” for putting a price on a license: “First you assess how much value is created if the partnership is successful. Then you put a value on what each partner is contributing and split the profits accordingly.”

Timing is everything. Alex McPherson, the veteran former CEO and founder in 1991 of the cancer vaccine company BioMira, explains, “The price of a license depends on how far advanced the product is in terms of development: 90% more for a product that has 10% risk, or 10% for a product that comes with a 90% risk.” Typically, biotechs

look to find partners somewhere in between those two extremes, after Phase II trials.

Ed Taylor, BioMira’s interim CEO, describes the initial deal with Merck & Co. as “A 50:50 co-promotional deal for our cancer drug, Theratope. We had the market for the U.S., and Merck would take Europe. It was the first step in our becoming a fully integrated

Introducing the leaders of the Mazankowski Alberta Heart Institute



**A renowned cardiologist.
An accomplished scientist.
A skilled cardiac surgeon.**

Clockwise from bottom right, Dr. David Johnstone - Clinical Director, Dr. Gary Lopaschuk - Scientific Director, Dr. Arvind Koshal - Director of Development & External Affairs

Edmonton’s Capital Health, with the University of Alberta, is proud to introduce a dynamic new leadership team for the Mazankowski Alberta Heart Institute.

Clinical Director Dr. David Johnstone, a nationally renowned cardiologist specializing in cardiac best practices and outcomes, will lead the heart care team in the new facility, providing leading-edge treatment and training for the next generation of health care providers.

Accomplished scientist Dr. Gary Lopaschuk is a world leader in the area of molecular heart science and energy metabolism. As Scientific Director, Dr. Lopaschuk will further develop the research that pushes the frontier of what is possible in preventing and treating heart disease.

Dr. Arvind Koshal, a skilled cardiovascular surgeon, is the head of a nationally recognized cardiac surgery program and a leading regional cardiac science program. As Director of Development and External Affairs, Dr. Koshal’s role reaches beyond the Institute’s walls into the community as well as nationally and internationally to extend the Institute’s contribution to the prevention and treatment of heart disease.

These exceptional leaders and the broader Alberta cardiac sciences team share the same singular and powerful goal: to better prevent heart disease and ensure Albertans have access to the best heart care in Canada.

The new Mazankowski Alberta Heart Institute will open in 2007 in Edmonton, Alberta.



biotech company." The opportunity collapsed when Theratope failed in Phase III trials.

"You want to keep some share of co-promotional deals. That's where the money is," advises Randall Yatscoff, CEO of Isotechnika, an Edmonton company creating a successor to cyclosporine, the organ-transplant rejection-inhibitor. "Otherwise, you end up with royalties amounting to 9% of profits and you'll watch shareholders sell your stock to buy companies that own marketing rights to your product."

Bootstrap Biotech

Most drug development is financed one of two ways: with the venture capital of patient investors or the development funding of a large pharmaceutical company in return for the license to manufacture the ultimate product. But when both forms of funding are scarce, some biotechs opt for a third source, revenue from contract research.

Edmonton-based Innovotech Inc. (formerly known as MBEC Bioproducts) conducts contract research into diseases like cystic fibrosis caused by biofilms – layers of mucous that host microbes. In the eyes of management, the strategy has two benefits. First, the research pays for further development of the company's proprietary product, an assay test kit used in the contract research itself. Second, Innovotech gets feedback on the kits. According to University of Calgary scientist-turned-CEO Ken Boutilier, "This is invaluable market research that keeps our finger on the pulse of how biofilm research is developing, so we build a knowledge base." Just as important, the scientists developing the kits also receive feedback. "It forces them to develop a business outlook: to ask themselves, 'What does the customer want and how much are they willing to pay for it?'" explains Boutilier.

When BioMira's lead drug Theratope failed in 2003, so did the company's hopes for a revenue stream to fund other products in its pipeline. So, to partly fund its next lead drug, Stimuvax, BioMira set up the Synthetic Biologics Unit in 2005 to produce, distribute and license chemically synthesised virus-

Ultimately, making money depends on the marketplace mix, branding and pricing. Branding is complex and depends on a wealth of knowledge and creativity – skills that Alberta companies recognize they lack, but partners can bring to the table.

When it comes to pricing, QLT founder and chair Julia Levy describes the art as "Not a very admirable process. You charge what the market will bear, depending on the drug's monopoly." ViRexx's Marc Canton explains

and bacteria-like compounds that stimulate the body's immune system. These "synthetic biologics" are sold to other companies conducting non-competitive research on vaccines. "It's an opportunity to spin off a company which is part of our core business and generate income to reduce the burn," explains Ed Taylor, BioMira's interim CEO.

He expects the earnings potential to total \$20 million over the next 10 years, "which won't be significant, but it's not insignificant either."

Not all those who've tried to work their way through proprietary R&D are so sanguine, however. In 2000, two years after going public, Isotechnika Inc. set up a diagnostics arm, Isodiagnostika, to develop and sell a breath test for ulcers. But the kits did little to develop marketing skills in their core business of developing immunotherapies, so the returns for a lot of hard work were minimal. "We had to go to Korea to raise the money to run the product line," says Randall Yatscoff, president and CEO. "We tried other breath test kits for other diseases, but the potential from diagnostics is tiny." In 2005 the diagnostics division generated \$1.3 million sales but cost almost as much to run. The profits represent a tiny dent in Isotechnika's total \$22.5-million research and development spend.

In addition, venture capitalists, concerned as they are with time to market, often take a poor view of activities that distract from core business. The trick, for firms stuck in the middle, is to weigh whether, in addition to revenue, skills picked up while milking these alternative revenue streams are worth the effort.

the pricing formula in similarly cold-blooded terms: "When there is no other drug in your class to compare with, you look at the substitutes to find a price range. Which could be death, chemotherapy or comparable drugs for other similar diseases."

After years spent developing a drug, it will fail without marketing know-how. Taiga BioActives Inc., a small private company in Calgary, took a big fall when launching its natural cold sore remedy a year ago. Lacking a sales director, the company's initial results were dismal. Taiga responded by bringing in Bill Slater, a marketing specialist from packaged-goods giant Colgate Palmolive Company. The product was rebranded, repackaged and a specialist distributor in Toronto appointed. Sales for the first six months of 2006 have since climbed to \$43,544.

Sales cannot be an afterthought. Isotechnika's Raymond Yatscoff suggests, "Strategic decisions to set up a sales force need to be taken

ALBERTA'S PRODUCT PIPELINE AWAITS THE OUTCOME OF PIVOTAL TRIALS ON SIX NEW PRODUCTS OVER THE NEXT THREE TO FIVE YEARS.

two years before a product launch." But distribution deals with an established player may be the only affordable route, especially since "to maximize profits, you need a highly skilled, specialized sales force. It's expensive and can't be set up overnight," advises Boodram from the stock analyst's chair. When selling overseas, these factors are even more significant.

The dream of many biotech CEOs is to own its own dedicated marketing team and sales force, thereby evolving into a fully integrated company such as California's Amgen Inc. or the multinational Pfizer Inc., which made \$10.8 billion in sales on cholesterol cutting drug Lipitor in its first year on the market in 1998. Closer to home, B.C.'s Angiotech Pharmaceuticals Inc. bought American Medical Instruments Holdings' sales and marketing force in March 2006, for \$785 million. No company in Alberta can afford that. Yet.

If confidence alone could sell a drug, then Clifford Giese is onto a blockbuster. Giese, the man behind the Mr Lube fast oil-change chain empire, is the chief executive officer of Edmonton's BioMS Medical. Giese is considering a variety of marketing partners but, "When there's no other drug for degenerative multiple sclerosis (MS) on the market and I can cover North America with six reps, I'll go it alone if I have to. It's my baby."

Giese's commitment is personal. "I wake up to insider information every day," he declares, referring to his wife Robin, whose MS has been kept at bay since she started taking the treatment in 1996 as part of a University of Alberta trial.

Likewise, most of Alberta's leading biotechs at least aim to keep control of manufacturing. But that does not mean manufacturing in-house. There is almost certainly no drug manufacturing industry in Alberta's future. If the leading companies here go into production at all, they will outsource to the rest of Canada and abroad. The strategy avoids an average \$20-million construction cost of a new facility.

"It used to be a joke on Bay Street," says David Cox, chief executive officer of TEC Edmonton, the government body set up to commercialize spin-offs out of the University of Alberta. For any biotech company to announce it was building its own production plant was the kiss of death, a prophecy fulfilled in the case of one of Alberta's first biotechs, Chembiomed Ltd. The company closed in 1991 partly due to the cost of constructing its own plant.

Whilst Alberta's biotech industry could survive perfectly well without a manufacturing base, long-term viability depends on the strength of each company's product pipeline. Post- and even pre-commercialization, stock analysts will be on the lookout for new applications of core technology capable of generating new revenue streams.

"You need to start developing a product every two years," judges Brad Thompson of Oncolytics, a Calgary-based company focused on developing cancer drugs. "If you don't have it, typically you'll buy into a Phase I product."

Buying in must be carefully executed, however. QLT spent \$500 million on in-licens-



CAN YOU MASS-PRODUCE THAT? There is no drug manufacturing industry in Alberta's future

ACROSS THE COUNTRY THERE ARE "TOO MANY, TOO SMALL AND TOO EARLY-STAGE COMPANIES," CONCLUDES ERNST AND YOUNG.

ing diverse drugs but had little expertise in developing or marketing many of those products. The company is also in court fighting a patent dispute over its lead drug Eligard. Levy admits the strategy "isn't doing too well."

In the short term, Alberta's product pipeline awaits the outcome of pivotal trials on six new products over the next three to five years. Some are brand-new "blockbuster" innovations, some less glamorous improvements on existing drugs. Long-term success, however, depends on "scientists concentrating on the next generation of 'me better' products, rather than pursuing 'the next big thing,'" believes TEC Edmonton's David Cox.

Brad Thompson of Oncolytics agrees. "In Alberta we shouldn't be trying to figure out how to get the big-pharma returns. Ninety-five per cent of companies doing that never get to profitability. The model that leads to the highest profitability is not to take a product across the finish line first."

Collectively, though, the industry could

do with a runaway hit. "One or two success stories is all that's needed to put Alberta's industry on the map and open the gates to greater investment," proclaims BioMira's Ed Taylor. "It's a matter of time," agrees Boodram. "Alberta is growing up. It was just slower to the game than B.C. where profits in QLT and Angiotech were pumped back into biotech, so now there's a healthy cluster."

Until then, success, lies in "virtual companies," according to Ryan Radke at BioAlberta – in other words, firms that develop drugs and arrange their financing by "sharing the risks, profits, manufacturing and marketing with experienced partners."

Which means that, "By the time you get a product to market," says Ed Taylor of BioMira, "the reality is you've had to give up control regardless."

However bitter a pill that may be to swallow, Alberta's baby biotech companies will have to share until they can stand on their own two feet, and only then stand up to the big guys. AV