

u.s. public markets

The third quarter of 2008 ran a remarkable course, with world attention moving quickly from the success of the Beijing Olympics to the unprecedented turbulence resulting from the credit bubble.

In the life science sector, the stock market performance of high-quality biotech companies held steady as the broader market began to decline in June, and the best biotechs continued to hold their value as stock markets crashed during the third quarter. The Nasdaq Biotechnology Index, comprised of

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venture capital

Preliminary data on the North American venture investment market indicate that during the third quarter of 2008 the rate of investment remained stable: the flow of capital into venture-backed companies during Q3 was within the same range as the past couple of years, and above the levels of the 2003-2006 period. During the third quarter the total venture industry appears to have invested approximately \$7 billion, down somewhat from the second quarter's \$7.7 billion (Source: Thompson and the NVCA). The "stability" in the funding levels in Q3, despite the public market turmoil, is actually not surprising and for those who can remember back to the collapse of the internet bubble of 2001, VC financing activity and valuation decreases lagged the public markets by about 6 months. We think there was a material amount of learning from that experience and we might expect to see a quicker response this time from VCs.

In the life sciences VC market approximately \$2.3 billion was invested in the third quarter, up slightly from the second quarter's \$2.1 billion (Source: Thompson and NVCA). Life Science investing represented one third of all the VC dollars invested during Q3, and one quarter of all the deals done by VCs. Year to date through the third quarter, life science VCs invested \$6.6 billion, down 8% when compared with the same period in 2007.

This slight drop in life science VC investment to date in 2008

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the road to liquidity

Value in the bioscience sector continues to be driven by a wave of strategic acquisitions by pharma and biotech buyers, and the third quarter was strong for life science M&A despite falling confidence elsewhere in the economy.

The overall M&A numbers in life science naturally vary from quarter to quarter, but the results for the third quarter were within the same range as we have seen over the last several quarters. If we include deals of all sizes, the 55 M&A deals announced during the third quarter represented a total dis-

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quarterly deal highlights

This quarter we chose to highlight four transactions that speak to some of the major themes we see in the life science venture market.

The first two, the acquisitions of Arius Research and Direvo, are further examples of the industry consolidation underway around protein engineering platforms like that of our recently acquired portfolio company **Morphotek**. In July **Roche Phar-**

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life sciences in Canada

It appears that there has been a lot of concern about the future of the life sciences / healthcare industry in Canada, but to date we had not been able to find anyone to quantify the issue and the opportunity, so we decided to do it ourselves. We used several different approaches including looking at Canadian public markets as a one proxy for the broader Canadian industry, examining year-over-year data for private company financings in the sector, and finally analyzing Canadian versus U.S. financing trends.

All the approaches tell the same story, **that the financing infrastructure for the Canadian life sciences industry is in crisis**, which means that the opportunity for smart, committed, deeply domain-knowledgeable and experienced investors has

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partner profile

Based in Lumira Capital's Montreal office, Daniel focuses on mid to late-stage opportunities in the therapeutics and medical device sectors. Daniel brings to Lumira over 20 years of investment, managerial, operational and consulting experience.



Prior to joining the firm in 2005, Daniel spent 10 years at **Shire Pharmaceuticals Inc.** and **Biochem Pharma Inc.** (acquired by Shire) as Vice-President, Business Development and Vice-President, Corporate Development respectively. Daniel was responsible for in-licensing and acquiring products and technologies in several therapeutic areas including anti-infectives, CNS, GI and oncology. He was also responsible for several private and public financing and M&A transactions in the therapeutics, vaccines and diagnostics sectors. At Biochem Pharma, he was a member of the Product Portfolio Committee and represented the Company on the Steering Committee of Research Collaborations. He also represented Biochem on the Board of investee companies. Prior to joining Biochem Pharma, Daniel was an investment banker at a large Canadian investment bank where he was involved in a wide range of M&A and financing transactions.

Daniel holds an M.D. from Université de Sherbrooke and completed his internship training at Montreal Jewish General Hospital, a McGill University affiliated teaching hospital. He also holds an MBA from Ecole des Hautes Etudes Commerciales in Montreal. His current and past investment responsibilities include: Resonant Medical, Neuromed and Excel-Tech Ltd.

"Outside of work, I venture down the snowy slopes of my favorite local ski resorts or enjoy cycling the back roads of the Eastern Townships. I enjoy Burgundies, love London (UK) and cheer for the greatest hockey team in the NHL..."

public markets

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the strongest biotech issues, **actually rose by 5.2% through the third quarter resulting in flat performance on a year to date basis. This was in stark contrast to the Nasdaq Composite Index which was down 10% in Q3 and 22% year-to-date. The S&P 500 Index was down 9% in the third quarter and 21% year to date.**

Biotech sector financings in the third quarter remained consistent with the first two quarters of 2008. Overall the biotech sector raised \$5 billion during the third quarter, the largest quarterly amount raised so far this year (source: BioCentury). This relatively steady state was however at a lower level than in previous years since the \$11.7 billion raised by the biotech sector during the first three quarters of 2008 is tracking at about half the \$30 billion raised in 2007. It appears that generalist investors are continuing to leave the biotech sector and as a result, capital deployment decisions are increasingly made by specialist investors including VCs. The venture component of total biotech financing has remained relatively consistent at between \$1.5 billion and \$2 billion per quarter over the past two years, while other sources of financing (IPOs, follow-on public offerings, and debt) have fallen.

The public equity market for bioscience companies has, in our view, become very selective. It now admits only those companies with a clear value proposition. There were no biotech IPOs during the third quarter (although there appear to have been no venture-backed IPOs of any kind in the quarter).

As in previous quarters the "good news" in terms of sector performance was segmented:

- Micro-cap companies with valuations below \$200 million got crushed - down 23% during the third quarter and down 48% since the beginning of the year. **In fact, there are about 160 public biotech companies with a market cap lower than \$50 million and less than 12 months cash** (Source: BioCentury) **suggesting that good opportunities may exist on the buy side.**
- The highest-quality bioscience companies were largely untouched, with mid-cap biotech companies (with valuations between \$500 million and \$1 billion) up an average of 15% during the third quarter. The highest-quality biotech names also benefited from a "flight to quality" element in the market. During the quarter Lumira Capital portfolio companies, **Pharmasset (Nasdaq: VRUS)** and **Alexza Pharmaceuticals (Nasdaq: ALXA)** both outperformed the Nasdaq Biotech Index, growing in value by 11% and 25% respectively on positive clinical trial news. **Pharmasset in fact ended the third quarter up 143% from its IPO price, and was the best-performing bioscience company in the IPO "class of 2007-8".**

portfolio company profile

KAI Pharmaceuticals

is a biology-based, product-driven biopharmaceutical company with clinical-stage programs addressing significant and unmet patient needs in cardiovascular disease, metabolic bone disease and pain. The company has applied its core expertise in the biology of protein kinase C (PKC) to discover highly potent and selective inhibitors and activators for validated PKC isozymes.



KAI's lead product, KAI-9803, is designed to reduce injury associated with ischemia and reperfusion in the settings of acute myocardial infarction (AMI), stroke, renal transplant and other ischemic conditions. Earlier this year KAI announced an exclusive agreement with **Bristol-Myers Squibb Company** for the global development and commercialization of KAI-9803, which is expected to enter Phase 2b clinical testing by the end of 2008 in patients with ST elevation myocardial infarction (STEMI). KAI received an upfront cash payment of \$25 million, and Bristol-Myers is funding the drug development costs, including the Phase 2b clinical trial. KAI may also receive from Bristol-Myers up to \$192 million in milestone payments based on the achievement of pre-specified development and regulatory milestones for KAI-9803. The FDA recently granted KAI-9803 Fast Track designation due to the significant unmet medical need for this indication.

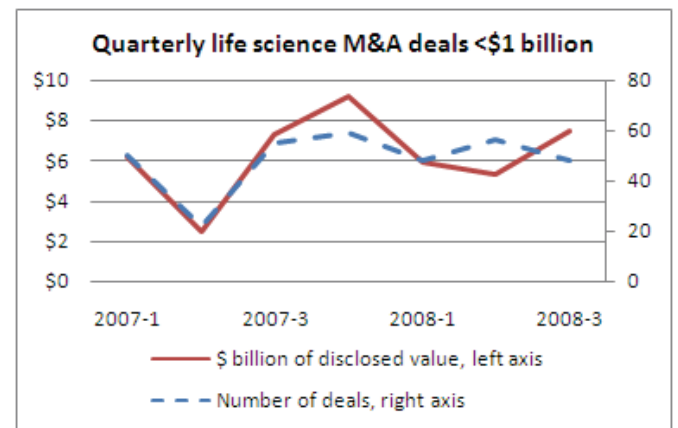
The company is led by its President and CEO, Steven James, who previously was the Senior Vice President of Commercial Operations at **Exelixis**. Steve has over twenty years of pharmaceutical, biotechnology and start-up experience in the life science industry, including senior positions at **Isis Pharmaceuticals** and **Sunesis**, where he was instrumental in raising venture and partner financing, as well as negotiating partnerships with major pharmaceutical companies. The company has assembled a very seasoned management team and a clinical advisory board experienced in making leading-edge discoveries and translating them into successful commercial products.

Lumira Capital is a major investor in KAI and participated in both the Series A and Series B financings which raised over \$60 million from well-established venture firms. Beni Rovinski manages the KAI relationship on behalf of Lumira Capital and also participates as an Observer on the Board of the company.

the road to liquidity

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closed value of \$26.3 billion (below prior year levels), but if we exclude the mega-deals above \$1 billion and focus on the segment of the M&A market that is more relevant to venture investors, there were 48 M&A deals that added up to a total disclosed value of \$7.5 billion (which was consistent with the prior year). Year-to-date for 2008 (excluding mega-deals), there were 153 deals for \$18.3 billion of disclosed value – up 20% in deal numbers and 17% in dollar value from the same period in 2007.



Of the M&A transactions where terms were disclosed (33 of the quarter's 48 deals below \$1 billion), the majority were all-cash deals. This continues a trend we have seen over the past three years where earn outs and other back-loaded structures are on the decline, from over 40% of all M&A deals in 2006 to below 25% so far in 2008 (Source: Windhover).

M&A exits, at least in the life sciences market, are increasingly bringing immediate liquidity.

ceo profile

Tony Falco, Ph.D., FCCPM is the President and co-founder of **Resonant Medical Inc.** which develops and manufactures 3D ultrasound image-guided adaptive radiotherapy products for cancer centers worldwide.



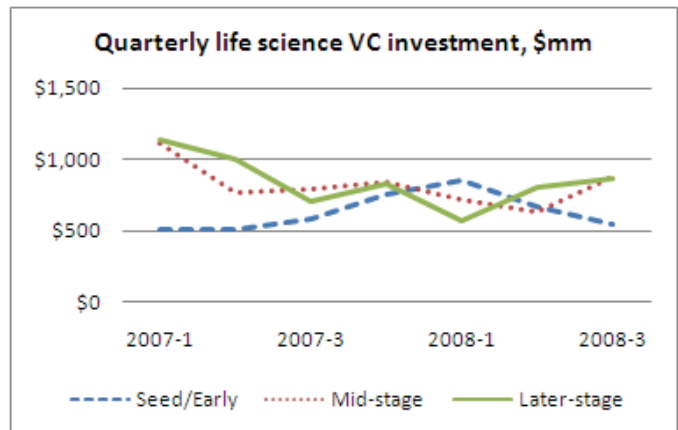
Dr. Falco has been instrumental in building the scientific, research and development foundation of the company since its beginnings in 2003 and he holds several patents whose principles are at the core of the company's products. As well as initiating the core intellectual property, he has also initiated and sustained Resonant's business development through clinical opinion-leader partnerships with top academic centers such as the **McGill University Health Center, the British Columbia Cancer Agency, the Princess Margaret Hospital, the University of Pittsburgh, the Cleveland Clinic Foundation, the Beth Israel NY Continuum Health Partners, and the University of Maryland** just to name a few. These partnerships are crucial for the clinical validation of the product and for growing Resonant's business in the cancer care market. Moreover, with over 12 years of clinical, IP creation, product development and business experience, Dr. Falco's insights and ideas in the fields of radiotherapy and medical imaging physics, combined with his clinical understanding of patient planning and treatment ensure that the Company's products address customer needs while keeping in line with the overall direction of the radiation therapy market. For the work he has done while at Resonant, work which positively affects the lives of hundreds of cancer patients on a daily basis, Dr. Falco received the coveted INNOVATOR AWARD in October of 2006. This award was given by the Association of Industrial Research in Quebec (ADRIQ) which recognizes exceptional achievements of distinguished individuals for their notable contributions to the province's industrial development.

Prior to starting Resonant, Dr. Falco practiced clinically at the McGill University Health Center and instructed as a Professor Member of the McGill University Faculty of Medicine. As a clinical medical physicist, he gained clinical and academic acclaim in radiation therapy and diagnostic imaging physics. In 2003, he earned the particular distinction of becoming the youngest Fellow in the history of the Canadian College of Physicists in Medicine. He has authored, or co-authored, numerous peer-reviewed publica-

venture capital

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is largely the result of a decline in early-stage investing. Seed / early, mid-stage, and late-stage deals each represent roughly a third of all life science VC dollars, but the trend in the exact amounts reversed from 2007 to 2008. Throughout 2007 and into Q1 of 2008, the amount of the capital flowing into seed and early-stage deals grew while dollars flowing into mid-late stage deals declined. This trend reversed during 2008, as seed/early stage dollars dropped by 35% from the \$836 million peak in Q1 to an estimated \$544 million in Q3.



The trend was exactly the opposite for mid-late stage deals which grew by approximately 35%. While many interpretations are possible, we believe that this simply reflects VCs ensuring that they are focusing their resources on building the companies already in their portfolios. We would expect this trend to continue through the balance of 2008 and into the first half of 2009.

tions, grants, patents, and clinical trial protocols. He obtained his Ph.D. in physics with specialization in clinical medical physics from McGill University in 1999.



life sciences in Canada

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never been better. Let's look at the specifics.

The Public Markets: We looked at the financial health of approximately 160 publicly-traded Canadian health and life science companies. Here are some of the metrics that came out of the evaluation:

- There are just over 100 companies which have a market capitalization of less than \$30 million
- These 100 companies have an average cash position of 7 months with a total combined forecast cash need of approximately \$460 million for the coming 12 months
- If you look at all companies with market caps under \$100 million, the funding need moves up to \$856 million
- Year to date for the three quarters ended September 30, 2008, the public companies with market capitalization of less than \$100 million have announced less than \$200 million in new financings, leaving a \$260 million gap for the fourth quarter

In conclusion, publicly traded Canadian healthcare companies are facing a material funding gap with no resolution in sight.

Private Companies: In all of 2007, private Canadian biopharmaceutical and medtech companies raised just shy of \$600 million in financing from VCs (Source: Lumira Capital, Thompson, CVCA). Our YTD analysis for 2008 reveals about \$175 million in financing for 23 private healthcare companies (vs. \$425 million in the first three quarters of 2007). The quarter-over-quarter trend was also not surprisingly negative, with just a handful of private companies announcing financings totaling a paltry \$20 million (some of which was tranching). All of these financings were follow-ons and none of them appear to have attracted capital from new investors.

The other important takeaway with respect to private healthcare company financings, for both the quarter and the year-to-date, has been the dearth of later stage and "truly enabling financings deals", those that bring more than \$20 million in new cash to a company. While we observed 7 such deals with an average transaction size of \$43 million in the first three quarters of 2007, there have been only 4 to date in

2008, and the average transaction size has fallen to \$29 million—none of these types of financings occurred in Q3. **Interestingly all four of the larger transactions this year were led by foreign based investors**, in contrast to the prior year when Canadian based funds were able to lead about half the financings. The trend appears to highlight all too well the reality that there is little late stage capital left in Canada to lead and structure the kinds of deals that are required to help these companies achieve their promise and that these deals are being "cherry picked" by foreign investors better capitalized to act on these opportunities. At the same time, the lack of a lead role for Canadian VCs in these late stage transactions (which tend to come with very attractive pricing and structures in these kinds of markets) is likely to perpetuate the cycle of pain for limited partners and investors in those Canadian VCs which were instrumental in the earlier financings of these companies, but are now being materially diluted. Interestingly, the pace for PIPEs (VCs participating in public market financings) continued to improve in Q3 and we observed 5 public life science companies announcing \$50 million in financings. As the public pricing for many public Canadian life science companies has collapsed, many of these companies are looking more attractive than their private counterparts, and funders are able to strike fairly aggressive terms that include preferred shares and board control changes in some cases (exactly what we have argued for the past 12 months needs to happen).

US vs. Canada: Last year at this time financings for private Canadian biotech and medtech companies were running at about 6.3% of the \$7 billion deployed in the sector in the US. **This year to date, U.S. bio and medtech companies have attracted \$6.6 billion in new capital (slightly less than in the prior year) but financings for their Canadian peers has dropped to 2.7% of U.S. disbursements or less than half of the 6.3% in the prior year.**

While some of these companies in the Canadian healthcare sector (both public and private) should, and undoubtedly will not survive, the simple reality is there will also be a number of good companies that are going to be forced to make bad decisions in the coming 12 months: cutting programs, cutting key people, failing to file for IP protection in key jurisdictions, giving back product rights, cutting corners, selling prematurely and entering into partnerships with little or no leverage.

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conference update: ASTRO 2008

Will proton based radiation therapy be the next great treatment for cancer? Based upon the exhibit floor space taken by the few large proton therapy vendors at the 50th annual meeting of the **American Society for Therapeutic Radiation Oncology** - Still River Systems, IBA, Optivus - one might be tempted to believe this. To put this in perspective, we'll outline a brief history of radiotherapy. Europeans first discovered X-rays in 1895, soon after scientists observed that both x-rays and radium could be used to treat superficial skin diseases and for removal of hair. In the early to mid part of the 20th century, radiation sources such as radium, cobalt and newly developed x-ray tubes started to be used for cancers that were not treatable by surgery thus "radiotherapy" was the treatment of last hope for many with inoperable or recurrent tumors. Radar research led to the discovery of the medical linear accelerator (linac) in 1953 which opened the door to more accurate, higher energy and focused radiation beams to cure cancers such as Hodgkin's lymphoma and testicular cancer. During the 70's new methods using computers and sophisticated imaging modalities such as MRI, CT and PET were developed and used to more accurately target tumors.

The holy grail of radiation oncology today is to be able to shape the radiation beam to the exact shape and precisely locate the tumor to spare as much healthy tissue as possible. Back to proton therapy. As a radiation source, what is the advantage of

using protons vs. an x-ray or electron beam (a linac)? Proton beams can be tuned to only penetrate tissue to a certain depth and will release most of their energy near the end of their travels. This means that tissues beyond the limit of penetration will be spared -- great news! The trick therefore is to deliver the beams at a calculated energy so the protons do not penetrate too deep. In order to do this accurately the density of the tissues being penetrated must be known and thus the location and shape of structures surrounding the cancerous tissue must be precisely mapped. Many tumors, such as those found in the prostate, lung, breast and others will either move during treatment or the organ being treated (such as the prostate) can change shape and actually move between each radiation session.

Imaging modalities such as ultrasound (*Resonant Medical*, a Lumira portfolio company being a leader in ultrasound guidance), MRI and cone beam CT are increasingly being used before each treatment to more precisely locate these types of tumors. Surprisingly, no system is yet available to non-invasively determine the exact location of tumors in real time, termed "adaptive radiotherapy", as the radiation is being delivered. Several groups today are working on systems to address this using MRI in conjunction with radiation sources. These systems, once developed, will be transformative to the radiation oncology field.

lumira capital investment team



From left to right: Daniel Hetu, Jack Jenuth, Gerry Brunk, Peter van der Velden, Charles Trimble, Nandini Tandon, Beni Rovinski, Graysanne Bedell, Steve Cummings, Brian Underdown.

life sciences in Canada

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Conclusion: We believe the financing problem will only get worse in the coming year (or better if you have capital to invest and know how to deploy it wisely in the sector) since by any metric **at the current pace it is hard to imagine funding for the year ending at anything but 50% less than prior year levels.**

On the acquisition side of the equation, Q3 was highlighted by two interesting M&A deals in Canada. The first was **Biovail Corporation** completing the acquisition of **Prestwick Pharmaceuticals**, based in Washington, DC for US\$100 million. The acquisition followed Biovail's announcement earlier in the year to refocus the firm in the CNS sector where Prestwick plays. This product-based specialty pharmaceutical company is engaged in the development and marketing of small molecule drugs for chronic diseases of the central nervous system.

The second deal of note was **Roche Pharma's** acquisition of **Arius Research** for CDN\$191 million. The deal comes on the heels of Roche closing several other strategic acquisitions this year including: RNAi company **Mirus** for \$125 million, sequencing firm **454 Life Sciences** for \$155 million, immunochemistry tools company **BioVeris** for \$600 million, PI3-K inhibitors company **Piramed** for \$160 million and DNA microarray firm **Nimble** for \$272 million (and lest we forget, buying out for \$44 billion the balance of **Genentech** that it did not already own). The Arius acquisition gives Roche the screening platform FunctionFIRST for antibody therapeutics, as well as a large library of antibodies for development initially in the areas of oncology and inflammatory diseases.

quarterly deal highlights

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maceuticals paid \$190 million in cash to acquire Canadian-based **Arius Research Inc.** for its monoclonal antibody platform. The price, a 25% premium to then-trading price of the company's shares on the TSX, represented a handsome return for the venture investors who participated in the Company's April 2006 \$21 million PIPE offering.

Direvo, a private European biologics platform company founded in 2000 was acquired in September 2008 by Bayer for \$300 million in cash, or 7.1x the raised \$42mm from a number of venture firms led by TVM Capital, (one of Lumira Capital's frequent syndicate partners).

In September, **Medtronic** agreed to acquire the Canadian medical device company **Cryocath (TSX: CYT)** for C\$400 million in cash, a 97% premium to the closing share price at the time of the announcement. Taking into account the venture financing that Cryocath raised from venture funds including ones previously managed by Lumira Capital, as well as the total public funding raised via its IPO and subsequent follow-on financings, this exit represents a return of nearly three times the invested capital.

Finally, and we don't see this often enough, emerging Canadian biotech **Microbix Biosystems (TSX: MBX)** acquired all of the inventory, IP, regulatory filings and related assets around urokinase from U.S. biotech company ImaRx (Nasdaq: IMRX) which had previously acquired these assets from **Abbott**. While not without risk, the acquisition consolidates Microbix's position in the urokinase business and this could be game-changing for the company in the coming year. In the interests of full disclosure, Lumira Capital participated in advising the company with respect to the acquisition.



Built on a foundation that leverages 18 years of experience as one of North America's leading healthcare and life science venture capital investors, Lumira Capital is the successor business to MDS Capital. During the past five years Lumira Capital's partners have helped build over 50 companies and the team currently manages over \$350 million of capital in three funds. Recent successes include the acquisitions of portfolio

companies such as Morphotek, (by Eisai Co.), and Corus Pharma (by Gilead Sciences) as well as the IPOs of Alexza Pharmaceuticals, Replidyne, Pharmasset and MAKO Surgical. Other portfolio companies and recent investments include Argos Therapeutics, Archemix, Cervelo, Ception Therapeutics, and Spinal Kinetics. Lumira Capital invests primarily in North American emerging-stage biopharmaceutical and medical device companies and has offices in Canada and the U.S. www.lumiracapital.com

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