

j.p. morgan healthcare conference

For 27 years, the annual JP Morgan Healthcare Conference in early January has been the seminal investor conference for the pharmaceutical and healthcare industry, and helps preview investor sentiment in our industry for the coming year. **This year's conference began and ended on a surprisingly upbeat mood, given the recent turmoil in worldwide markets.** Four thousand attendees gathered at the St. Francis hotel, together with an estimated ten thousand others

(Continued on page 4)

life sciences in canada

Is there a funding gap in venture and institutional investing in the Canadian private health and life sciences sector? The short answer, as you may imagine, is yes! We estimate that **the size of the funding gap in Canada from 2004-2008 has grown to roughly \$2 billion, and that virtually 100% of this gap has been attributable to "later stage" life science companies.** Perhaps a bit of a surprise for those who argue the need for more early stage capital, so let's look at the data:

During the period 2004-2008, and using a 1:10 ratio as our guide, Canadian and U.S. VC's invested relatively equivalent

(Continued on page 5)

u.s. public markets

In the public market for U.S. life science companies, the end of 2008 reinforced three themes:

Biopharma companies with (a) relatively de-risked technologies and/or products, (b) that have a near-term path to the marketplace, and (c) that are well capitalized or are highly financeable, significantly outperformed the broader equity market.

The NASDAQ Biotechnology Index was down 15% in the fourth quarter and for the year 2008, which compared very positively against the NASDAQ Composite Index (down 21%

(Continued on page 2)

venture capital

The venture capital industry ended 2008 much as we predicted, on a downward trend for new investments. Venture capitalists as a whole invested \$5.4 billion across all industries during the fourth quarter of 2008, down from the \$7-8 billion per quarter range we saw earlier in the year. The total for 2008 was \$28.3 billion invested, down 8% from 2007, but still higher than any of the previous three years.

As in previous years, the life sciences sector represented about one third of the total venture industry in terms of capital deployed during 2008. Life science-focused venture funds invested \$1.7 billion during the fourth quarter, down from the \$2-\$2.3 billion per quarter invested through the earlier part of the year. Investment activity for all stages of investment was off in the 4th quarter and (from speaking to our peers) we would expect to see a dramatic drop-off in series A financings in the next couple of quarters as investors "hunker down" and look to support their existing companies. Interestingly, evidence to support this thesis is already emerging as "later stage" companies, which have typically attracted 40-60% of their capital from new investors, saw Q4 contributions from new investors drop to a historically low 24% (Source: Thompson Financial).

What are the implications? Investors will have to retain more capital to support their existing portfolios and, by definition, will have less capital available for new ideas and opportunities. Emerging companies without strong investor syndicates are likely to be in deep trouble in the upcoming couple of quarters and VC's who have not allocated adequate capital

(Continued on page 3)

quarterly deal highlights

The Israeli life science and medical technology sector is an example of how value that can be created in an economy that is a fraction of the size of Canada's when research, entrepreneurial drive, and investment come into alignment.

This past quarter two Israeli companies, one a biologics manufacturer and the other a cardiology devices and image-guided surgery company, were acquired for over \$730 million.

(Continued on page 3)

partner profile

Focused on companies with innovative therapeutic products, Brian's career has touched all phases of the cycle that begins with discovery to translation of ideas into products. Brian has been with Lumira Capital for 11 years and has been involved in starting and building companies both in Canada and the U.S. in a broad range of therapeutic areas with a special emphasis on immunity, cancer and inflammation. Among the companies that Brian has been intimately involved with are: Argos Therapeutics, Ception Therapeutics, Cytochroma Inc., ID Biomedical and Trillium Therapeutics.



Brian Underdown

Prior to joining Lumira Capital, Brian was a senior executive at Pasteur Merieux Connaught (PMC) where he was responsible for several vaccine development programs and participated in global corporate committees with oversight of PMC's R&D portfolio. In addition, he was responsible for PMC's funding program with research groups in Canadian universities, an activity that allowed him to leverage his extensive experience as a senior researcher and faculty administrator in two of Canada's leading universities, McMaster and the University of Toronto.

Brian still enjoys close contact with the academic community and has served on a number of grants committees of the Canadian Institute of Health Research and the Boards of National and Provincial Networks of Centres of Excellence in the area of vaccines, allergic diseases and genomics. Brian holds a Ph.D. from McGill University followed by a post-doctoral stint at Washington University.

"Perhaps my greatest influences are from my early days in scouting where teamwork was a primary value and is so important to successfully building companies. My recreational canon includes travel, probably fostered by those great years as an academic with sabbaticals and international meetings of the scientific tribe and canoeing, where a sunset and a campfire is about as good as it gets"

u.s. public markets

(Continued from page 1)

in the fourth quarter and 41% for the year) and the S&P 500 (down 18% for Q4 and 39% for the year). In Lumira Capital's portfolio, Pharmasset (NASDAQ:VRUS) was one of the stronger performers in the NASDAQ Biotech Index. While VRUS ended the year flat, it had enjoyed a dramatic price surge early in the year and is up 60% since its 2007 IPO.

Small cap biopharma companies with less visibility to product approvals, and weaker finances, underperformed the broader equity market. For companies entering the period with a market cap below \$200 million, average share price performance was negative 39% in Q4 and negative 67% for the year (source: BioCentury). **Many of these companies represent compelling investment opportunities for those with capital to invest and the domain knowledge to find undervalued assets.**

Generalist investors have largely left the biopharma sector and, as we have seen through most of 2008, the trend has been for more and more equity capital in the sector being deployed by specialist life science investors. Of the \$13.5 billion invested in the biopharma market (including public companies) in 2008, debt and other investment vehicles accounted for 47% (\$6.3 billion), while venture investors deployed 40% of the 2008 total (\$5.3 billion). Public equity investment (IPO and follow-ons) amounted to 15% of the year's investment (\$2 billion) (Source: BioCentury).

The most obvious change in capital flows was with respect to IPOs. Only 4 healthcare/life science companies managed successful IPOs in 2008 and we were very pleased that our portfolio company MAKO Surgical was one of them. MAKO followed up with a \$60 million follow-on financing in Q4. The dearth of IPO activity is expected to continue in 2009. But with big pharma CEOs making comments like those below, the window for high value partnerships (i.e. non-dilutive capital) and M&A (i.e. exits independent of IPOs) for venture-backed life science companies is outstanding:

Merck CEO Richard Clark pegs acquisitions as a priority for 2009. The company has the resources to make "whatever investments are needed," the exec told analysts and investors at a Goldman Sachs conference yesterday. Clark also said that "strategic opportunities"--including deals--are key for the year ahead, Dow Jones - 2009

Andrew Witty at GlaxoSmithKline and Bernard Pousset at Wyeth have already said they are suspending share buybacks to take advantage of the dislocation in the markets and to acquire assets. Financial Times - January 5, 2009

portfolio company profile

Archemix Corp. is a biotechnology company focused on discovering, developing and commercializing aptamer therapeutics.



Aptamers are synthesized oligonucleotides, or short nucleic acid sequences, that bind to proteins with high affinity and specificity and represent a potentially new class of therapeutics. Using Archemix's processes for discovering aptamers, which are protected by its broad patent portfolio, Archemix is developing aptamer product candidates for rare haematological diseases. In addition, Archemix has licensed its intellectual property to third parties to develop their own aptamer product candidates in other areas. Currently, Archemix's licensees are evaluating five different aptamer product candidates in human clinical trials; two in Phase 2 and three in Phase 1. Archemix has additional partnerships with several pharmaceutical and biotechnology companies, including Merck Serono, Pfizer, Takeda, Eli Lilly and Isis Pharmaceuticals.

On December 23, 2008, Archemix and GlaxoSmith-Kline (GSK) announced a worldwide strategic alliance to discover, develop and commercialize aptamer therapeutics to treat inflammatory diseases, such as rheumatoid arthritis and inflammatory bowel disease. Under the terms of the agreement, Archemix will receive \$27.5 million in upfront payments from GSK and stands to receive up to \$1.4 billion in additional payments should various product milestones be met during the partnership. This alliance represents the largest industry deal in 2008 and the second largest pharma/biotech alliance ever in terms of potential value.

Lumira Capital invested in the Series A financing of Archemix, which has not needed to raise venture capital funding since 2004. Gerry Brunk manages the relationship with Archemix, which is located next to Lumira Capital's office in Cambridge, Massachusetts. He participates on Archemix's Product Development Board.

venture capital

(Continued from page 1)

reserves are likely to encounter material declines in value as their portfolio companies are forced to complete highly dilutive financings, sell pre-maturely or fail altogether. This will definitely be a "haves" and "have-nots" market.

Despite the decrease in 2008, investment activity as a whole in life sciences was up over the previous five years. This was not true for all other venture asset classes. While the present economic and financial environments mean that no asset class is out of the woods, two fundamental features of the life sciences venture market suggest that experienced venture funds can build value and reward their investors in the coming years:

- A declining valuation environment for companies that are in the "sweet spot" for venture financing, and
- strong market drivers that are anticipated to support high value exit realizations for companies with de-risked assets needed by big pharma and biotech - a feature largely unique to the biopharmaceutical industry.

quarterly deal highlights

(Continued from page 1)

In the first transaction, Johnson & Johnson acquired Omrix (NASDAQ:OMRI), a producer of proprietary biological products including surgical adhesives, immunoglobulins, and other human plasma derivatives. JNJ paid \$438 million for Omrix, representing a premium of 24% over the market price of the Omrix's shares. The acquisition price was 7.1 times Omrix's 2007 revenue, and 37 times earnings.

In the second transaction that we highlight this quarter, St. Jude Medical (NYSE:STJ), a medical technology and services company with a market value of \$12 billion, acquired MediGuide for \$300 million. MediGuide develops technology for image-guided navigation of interventional cardiology devices within the body. In terms of company stage, MediGuide was at the point where medtech companies are often acquired: its lead product was approved for sale in Europe and was being testing in the U.S. under investigational device exemption (IDE) clearance.

Although biopharma acquisitions often have a higher profile because of the premiums being paid as a function of the restructuring of the pharma industry, MediGuide reminds us that **medical device companies which are truly innovative and game changing** are also being acquired and commanding high valuation multiples. MediGuide was St. Jude Medical's fourth cardiology device acquisition in 2008.

ceo profile

Mr. Tullman is co-founder, President and CEO of Ception Therapeutics. Ception was built on good timing, clear vision and expert diligence. With a combination of confident insight for its lead asset, a world class and highly experienced team and top tier investors, Mr Tullman has led Ception to its recent deal with Cephalon. Ception received an upfront payment of \$100 million for a purchase option agreement. Cephalon can exercise its option and purchase Ception's outstanding capital stock for \$250 million, plus additional payments for clinical and regulatory milestones.



Steve Tullman

Prior to the formation of Ception, he co-founded Trigenesis Therapeutics, which was acquired in 2004. Steve is also a co-founder and Director of the PreSun® Company, a privately held dermatology company.

He began his professional career in the pharmaceutical industry at SmithKline Beecham (now GlaxoSmithKline). During his fourteen years with that company he accumulated broad industry experience in finance, sales, marketing, research and development. Steve held key positions including the head of GSK's Global Commercial Strategy for the Musculoskeletal, Inflammation and Dermatology Therapeutic Areas including all assets from discovery through marketed products. He also led Global Commercial Strategy as Director for Respiratory New Product Development, International Marketing Director for the Philippines, Associate Director for Anti-infective Products and Global Brand Director for Bactroban®, Senior Global Marketing Research Manager and Manager of Business Development Analysis. He has worked overseas, living in the UK and in South East Asia and has many years of overall global commercial development responsibility.

He received his Bachelors of Science Degree from Rutgers University in New Jersey.

j.p morgan

(Continued from page 1)

not formally registered, to hear updates from over 330 public and private companies. Five of us from Lumira Capital attended the conference, where we focused on meetings with portfolio companies, co-investors, licensing and business development groups from many of the large companies, and M&A bankers from various firms. In addition to formal J.P. Morgan-sponsored events, dinners and cocktail receptions for the venture capital community hosted by groups such as Johnson & Johnson, Pfizer, Lazard, Roche and Pacific Growth Equities were also well-attended.

The optimism emerging from this year's conference springs from three observations highlighted throughout the week:

- M&A to Drive Venture Capital Liquidity.** Acquisitions and consolidation are expected to increase pace, to the benefit of venture-backed companies. Established firms are cash-rich and product-poor (the top 10 pharma companies have over \$100 billion cash on hand at year end); they need to acquire companies to drive revenue growth that their internal R&D efforts have been unable to support. Bankers estimate the European and U.S. pharmaceutical sector will collectively generate \$440 billion in operating cash from 2008-2011, providing substantial internal resources for funding acquisitions. This is no longer a "nice-to-have"; acquisitions are fundamental to survival. Supporting this notion, attendance from members of the business development and M&A groups of all the large and medium-sized pharmaceutical firms, biotechnology companies and med-tech firms was reported by J.P. Morgan to be twice last year's level, and the largest ever in the 27-year history of the conference.
- Innovation Continues to be Highly Valued.** A new administration in the U.S. is viewed as a net-positive for our industry. Science and technology innovation have a new friend in the White House. Calls for cost containment in all healthcare systems worldwide put added pressure on established companies with "me-too" products to invest in and acquire emerging companies developing novel, innovative products that address true unmet medical needs. These are exactly the type of companies venture investors help build.
- Uniquely Positive Time for Venture Investing.** As long-time attendees of this conference, we have seen cycles of market ups and down. We left this year's conference sharing what many of the co-investors we work with also told us last week: that times of uncertainty and market transformation have typically produced terrific opportunities for venture capital investors. We recognize many old patterns in the current set of forces shaping our industry that leave us extremely excited to be investors in this sector.

(Continued on page 6)

life sciences in canada

(Continued from page 1)

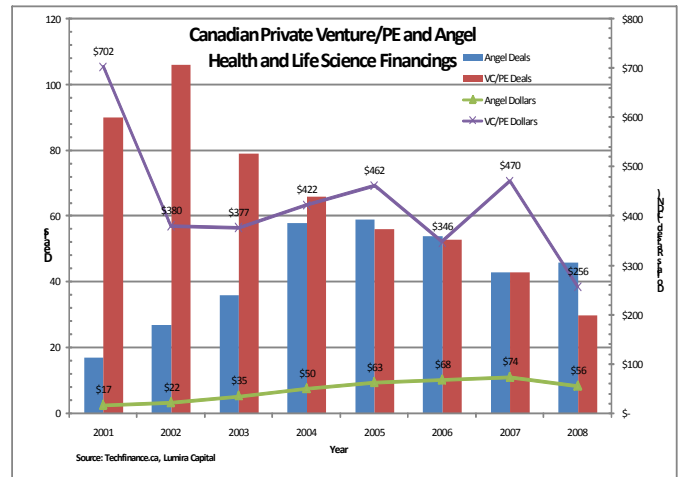
Funding Gap in Canadian VC - Health and Life Sciences				
2004 - 2008				
	USA(M)	Canada(M)**	% of USA	Shortfall [^]
Total invested	\$ 38,708	\$ 1,870	4.83%	\$ (2,001)
Early Stage	\$ 9,463	\$ 1,025	10.83%	\$ 78
Late Stage	\$ 28,958	\$ 846	2.92%	\$ (2,050)
Ratio of Late to Early Stage	3.06 [†]	0.83 [†]		
Predicted Late stage funding***	\$ 28,958	\$ 3,135		
Shortfall in Late Stage funding		\$ (2,289)		

[†] Source: Thomson Financial - VentureSource
^{**} Source: Techfinance.ca, Lumira Capital
^{***} Based on the Canadian economy being 10% of the US.
[^] Based on using the US ratio of late to early stage dollars invested

amounts in early-stage private health and life sciences companies (actually at 11% of the U.S investment levels, Canadian investments were slightly above expectation). **For later-stage companies, however, investment in Canadian companies was a mere 3% of that in the USA.** While we have fundamentally believed and argued this point for years, the data likely come as a material surprise for many who have argued or believed investments in Canada were particularly lacking in the early stages. For every dollar invested in early stage companies in the U.S., roughly three dollars are invested to move the most promising innovations up the value chain. In Canada, it appears that the ratio is less than 1:1, i.e. for each early stage dollar less than one dollar is invested at the later stages. As you can imagine, this simply makes no sense since 75-80% of the capital required to build a successful life sciences company is needed for later-stage development expenditures.

So what's going on? It is certainly not due to a lack of innovation in Canada. The Toronto region, for example, is home to the 3rd largest biotechnology cluster in North America and Ontario is home to over 800 life science companies, employing over 40,000 people which generate more than \$11 billion in annual revenues (Source: Ontario Ministry of Research and Innovation - Ontario's Biopharma Cluster, June 2008). It is also not related to an inability to attract the best and brightest scientists to Canada. In fact "BUSHENOMICS" have been very good for driving many of the best to want to practice their trade at Canadian academic centres. Taking the best early-stage companies in Canada to the next level requires late stage funding from sophisticated institutional investors who are domiciled in Canada but have the reach, experience and relationships to help build truly North American companies by helping to attract highly-experienced management teams, foreign dollars, and the right commercial partners. From this will come the high-value exits, the spin-out teams and the assets that will underpin the next wave of innovation and company formation.

Total disbursements to Canadian health and life sciences companies in 2008 were down a shocking 68% compared to 2007, (\$652 million vs. \$2.01 billion). Investments in public companies came down 79% vs. 2007 (this is not a typo — \$302 vs. \$1460 million), and investments in private companies were down 59% (\$594 vs. \$351 million). For venture and angel-backed private companies disbursements were down 24% (\$56 vs. \$74 million) and 45% (\$256 vs. \$470 million) respectively. All-in-all the numbers are distressing. Ironi-



cally, this massive decline in value within the Canadian sector in 2008 has resulted in more and better investment opportunities than we have seen in many years. Having said that, this is not a time for generalists to wade into the sector with a portfolio strategy. **The key today is for sophisticated investors to identify the best platforms and then work with management and existing investors to ensure they develop a business plan and financing strategy that is sustainable through these markets. Band-aid financings and "more of the same" strategies will not work!**



biofinance 2009

As in past years, Lumira Capital is once again very pleased to be a sponsor of BioFinance which this year will be held in Toronto the 28-30th of April 2009 (see www.biofinance.ca for details)

As we thought about the role we should play at BioFinance this year, we concluded that it should be around highlighting the challenges, opportunities and rewards to be gained by investing in and building the next generation of biologics companies. Why this focus? — we are seeing increasing approval rates for large molecule products at the FDA, increasing recognition/evidence of biologics as a safe and highly efficacious modality for treating important diseases (affecting both large and small sectors of the population), and a rapidly accelerating recognition that biologics are likely to make up a growing proportion of the portfolio of products offered by big pharma to their patient and physician customers. In fact, in his communication to employees in January 2009, with respect to Pfizer's acquisition of Wyeth, Jeffrey B. Kindler, Chairman and CEO of Pfizer said among other things:

"Within three years, we expect that approximately 30 percent of our revenues will be generated by businesses outside of small-molecule pharmaceuticals" – in other words biologics.

Owing to Canada's deep franchise and long history of success in biologics, we believe that an opportunity for Canadian entrepreneurs, scientists and investors to participate in this field has never been better. To help us all better understand these opportunities, Lumira Capital's invited speakers for BioFinance 2009 include:

Steve Tullman: (see CEO profile in this issue) who architected the highly creative structured sale of his company Ception to Cephalon in early January, 2009,

Errol De Souza: the CEO of Archemix (see Company profile in this issue) who architected the blockbuster licensing deal that his company announced with GSK in December of 2008, and

Fred Frank: the legendary investment banker who is Vice-Chairman, Lehman Brothers (Barclays) and has been an advisor to successful Lumira Capital companies such as Ception and Morphotek (acquired by Eisai Co. in 2007 for \$350 million)

j.p morgan

(Continued from page 4)

Three Lumira Capital portfolio companies were invited to make formal presentations during the J.P. Morgan conference: Alexza, Pharmasset, MAKO Surgical. In addition, Ception Therapeutics participated in Cephalon's formal presentation during which Cephalon announced its acquisition plans for Ception. Twelve Lumira Capital portfolio companies attended the conference and participated in meetings with potential investors, partners and acquirors throughout the week. Several of our portfolio companies also announced important news during this year's conference:

Ception Therapeutics announced that Cephalon, a \$5B leading biotechnology company, has taken an option to acquire the company.

Alexza (NASDAQ: ALXA) elaborated on recently announced positive Phase 3 clinical data for the company's lead product and plans to submit the product for FDA approval in the next 12 months.

Pharmasset (NASDAQ: VRUS) announced FDA approval to begin Phase IIB clinical trials of R7128 for the treatment of Hepatitis C (in partnership with Roche). Upon the news, analysts increased their 12-month price target to as high as \$31.00 per share.

Archemix briefed investors on the company's \$1.4B potential value partnership with GSK that was announced before year end.

MAKO Surgical Corp. (NASDAQ: MAKO) announced 2008 4th quarter and full year sales, exceeding company guidance and analyst estimates for the third consecutive quarter as a public company.

2008 Portfolio Highlights

Liquidity



Announced acquisition by Cephalon Inc. in deal potentially worth over \$350 million.



Went public in \$51 million IPO, one of only seven venture-backed companies in any sector to go public in 2008. Raised an additional \$60 million in October follow-on offering and exceeded sales estimates in three consecutive quarters.



Announced merger with Cardiovascular Systems Inc. Resulting publicly listed company's revenue forecast estimates in 2009 to be over \$35 million.

Strategic Partnerships and Financing



Formed a broad alliance with GlaxoSmith-Kline for a potential value to Archemix of \$1.4 billion, the largest deal of 2008 and the second largest biotech/pharma alliance ever.



Raised \$35 million Series C financing.



Formed strategic distribution alliance with Millipore Corp.



Announced technology partnership with Siemens Healthcare.



Formed \$350 million global clinical & marketing partnership with Bristol-Myers Squibb. KAI advanced three product candidates into clinical trials, including two in Phase 2 studies.

Value Creating Milestones



Announced positive results from its second Phase 3 clinical trial of AZ-004. Five other product candidates advanced through Phase I or Phase II studies.



Received CE Mark approval to begin marketing in Europe and completed patient enrollment in clinical study that will form the basis for an FDA pivotal approval study.



Reported positive clinical efficacy and safety for Hepatitis C product and received FDA approval to begin Phase 2b study with partner Roche. Neared completion of enrollment for Phase 3 global registration approval studies for Hepatitis B product. Stock reached an all-time high of \$36 during 2008.



Introduced the Clarity™ Breast System, the world's first Image Guided Radiation Therapy solution for precise non-ionizing guidance for breast cancer treatments.



Completed enrollment of U.S. clinical trial. International sales of spinal disc implant grew 42%.



Built on a foundation that leverages 20 years of experience, Lumira Capital is one of North America's leading healthcare and life science venture capital investors. 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 Ception Therapeutics (by Cephalon), 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, Cardiac Dimensions, and Spinal Kinetics. Lumira Capital invests primarily in North American emerging-stage biopharmaceutical and medical device companies. Lumira Capital's portfolio companies are located throughout North America and the Company has offices in Canada and the U.S. www.lumiracapital.com

This report is based on information that we consider reliable, but we do not represent that it is accurate or complete, and it should not be relied upon as such.