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## Ten Years After – Looking Back At A Biotech Boom

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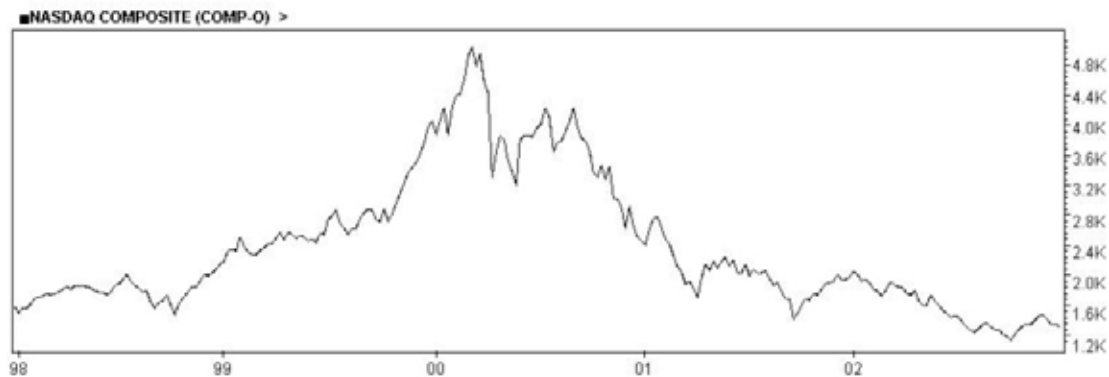
## Ten Years After – Looking Back At A Biotech Boom

### Introduction

There have historically been overlapping biotech booms and IPO windows, the three most recent boom/windows being 1995-1996, 1999-2001 and 2003-2005. Each of these boom/windows was impacted by positive external market forces, with the last two benefiting from the dot-com bubble and the post-9/11 market bounce, respectively. The driving factors within biotech have been different for each boom/window: 1995-1996 was partially driven by investor demand for new stories; 1999-2001 was driven by the potential for new technologies; and 2003-2005 was partially driven by product approvals and successful companies. In this report, we look back at the 1999-2001 boom/window, the IPOs and their subsequent performance.

### The External Trigger – The Dot-com Bubble

The dot-com bubble was a speculative e-commerce bubble, which started in the mid-1990s and peaked on March 10, 2000 when the NASDAQ reached its all-time high of 5,132. Traditional metrics for valuation such as P/E ratios were not used to value the new internet-based companies, which focused on growth and market share instead of revenues and earnings. The term “irrational exuberance” was used in a speech in 1996 by the then-Federal Reserve Board Chairman, Alan Greenspan, to describe a different economic situation but it is an appropriate description of the dot-com bubble. Since the business models of most e-commerce companies were not viable, the bubble burst as shown in the stock chart for the NASDAQ Composite Index. However, this bubble did create a large pool of capital, both private and public, with an appetite for risk and emerging technologies which had potential game-changing attributes.



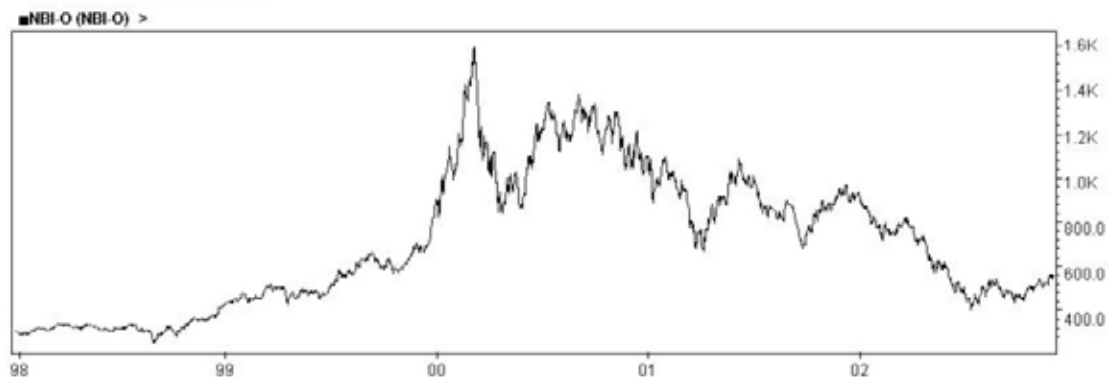
Source: TSX Connect

## The Internal Trigger – Genomics and Proteomics

The two emerging biotechnologies which had potential game-changing attributes that appealed to many dotcom investors were genomics and proteomics. The single event that grabbed public attention was the Human Genome Project, which produced a working draft of the genome in 2000 and a complete one in 2003. Genomics had the potential to increase the success rate during new drug development through increased understanding of which genes were involved in specific diseases and how they interacted with each other. Proteomics had similar potential by looking for the proteins which would be the best targets for drug development. Identifying genes and proteins turned out to be relatively easy, and also useful as genomics and proteomics both play critical roles today in new drug discovery. However, turning this information into profitable services or new products was very costly and time consuming and these new technologies failed to meet market expectations.

## The 1999-2001 Biotech Boom

Biotechnology suffered through a financing and valuation desert during 1997 and 1998 but climbed to dizzying heights in 2000. The extent of this boom can be seen in the chart for the NASDAQ Biotechnology Index, which peaked on March 7, 2000 and then collapsed along with the NASDAQ. Starting in mid-2000, the NASDAQ Biotechnology Index was more resilient and did not collapse as fast as the technology-based NASDAQ.

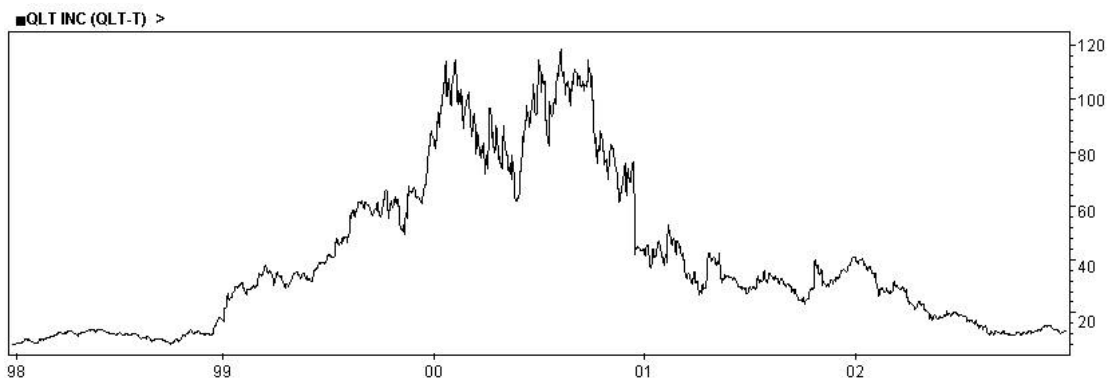


Source: TSX Connect

The extent of this boom can also be seen in the share price charts for drug discovery and clinical development stage companies. Many of these companies which were already public reached all-time high share prices in 2000 and also completed significant financings during this boom, illustrated by the following two examples.

Lorus Therapeutics acquired the private company GeneSense Technologies in October 1999 and simultaneously completed a \$10 million equity financing at \$0.33 per share. However, the intraday share price peaked on March 6 at \$8.80, a 2,567% increase from the prior financing price, and the market cap was about \$1 billion. In May 2000, Lorus completed a bought deal financing for \$46 million at \$3.00 per share.

QLT received aggregate net proceeds of \$188.3 million from a public share offering completed in May 1999 (US\$21.81 per share). Visudyne received approval from the U.S. FDA in April 2000 and the European Commission granted marketing authorization in July 2000. The QLT share price reached an all-time TSX high of \$120.00 on August 8, 2000. The NASDAQ share price peaked at US\$81.94 on August 7 and had previously reached US\$81.00 on February 8. Based on the 67.7 million shares outstanding at the end of 2000, the market cap peaked at about \$8.1 billion.



Source: TSX Connect

### Who Jumped Through The IPO Window?

The biotech boom also created an IPO window through which many private companies entered the public markets. There were three general types of IPOs: the VC-backed companies which completed larger offerings predominantly purchased by institutional funds; companies which completed smaller offerings often with substantial retail involvement; and companies which used an RTO (reverse take-over) of an existing public company, often a capital pool company (CPC). The IPO window actually stretched across a 3-year period, with most IPOs occurring in the middle, but starting with AnorMED in March 1999 and ending with BioMS in August 2001.

A total of \$296.5 million was raised by the group of eleven IPOs with minimum gross proceeds of \$10 million each. Within this group, only one IPO (Adherex) had a large retail involvement. Two attempted IPOs were withdrawn (Kinetek and Supratek) and the private company with the largest financing (\$82.5 million) in the Canadian sector, MDS Proteomics, never filed to go public. Within the other two groups, a key factor was the ability to do additional larger financings after becoming public. For example, Oncolytics Biotech's IPO was primarily a retail offering at \$0.85 per share to get an Alberta Stock Exchange listing, followed by an institutional financing in February 2000 at \$4.70 per share which allowed the company to obtain a TSX listing. In the RTO group, BioMS went public via a capital pool company transaction, listing on the CDNX and completing a financing later in 2001.

## Canadian Biotechnology IPO Class of 1999-2001

Company	Ticker	IPO Information			Notes
		Month/Year	Amount (\$ million)	Share or Unit Price	
<b>Financings (\$10 M+)</b>					
Nexia	NXB	December 2000	\$42.4	\$8.00	
CryoCath	CYT	October 2000	\$40.0	\$8.00	
Neurochem	NRM	June 2000	\$36.8	\$8.25	
Chromos	CHR	July 2000	\$34.5	\$8.00	
AnorMED	AOM	March 1999	\$31.5	\$6.10	
ConjuChem	CJC	November 2000	\$28.8	\$5.50	
GlycoDesign	GD	November 2000	\$25.0	\$11.75	
Ecopia	EIA	October 2000	\$20.8	\$1.80	1
ART Advanced Research	ARA	June 2000	\$16.7	\$9.00	
Cytovax	CYT	February 2001	\$10.0	\$6.00	
Adherex	AHX	June 2001	\$10.0	\$1.50	
		<b>Group Total</b>	<b>\$296.5</b>		
<b>Smaller Financings</b>					
					2
Waratah	WAR	September 2000	\$9.8	\$0.85	
Andromed	AD	March 2001	\$7.3	\$2.25	
Transition Therapeutics	TTH	February 2001	\$5.3	\$1.25	
ARIUS Research	ARI	March 2000	\$5.0	\$5.00	
Neptune Technologies	NTB	July 2001	\$5.0	\$1.00	
Genomics One	GNX	November 1999	\$3.8	\$1.25	
Oncolytics Biotech	ONC	October 1999	\$3.4	\$0.85	
BioMax	BIX	March 1999	\$2.2	\$1.25	
		<b>Group Total</b>	<b>\$41.8</b>		
<b>RTOs</b>					
					3
BioMS	MS	August 2001			
Bioxel	BIP	July 2001			
Medicure	MPH	November 1999			
MedMira	MIR	March 2000			
Pheromone Sciences	PHS	February 2000			

Source: Company reports and regulatory filings

Notes:

1. Ecopia raised \$20.8 million in a private placement in June and the TSX listing was in October.
2. Other healthcare companies which went public with smaller financings include DTI Dental Technologies (acquired), HeartLink (acquired), Stellar Pharmaceuticals (active), MediSystem (acquired) and Lasik Vision (acquired).
3. RTOs have been financed in various ways, including by private placements prior to or at the same time as the qualifying transaction or by financings shortly after the qualifying transaction.

## Ten Years After – Performance of the IPO Class of 1999-2001

There are two ways to look at the performance of this group of companies. First, with respect to the lead products at the time of the IPO, have those products now been approved, are they still progressing through clinical development, have there been development problems, and have they been replaced by other lead products?

- Mozobil, AnorMED's lead product when it was acquired by Genzyme, has subsequently been approved. However, AnorMED's lead product at the time of the IPO, a platinum-based cancer drug, ran into development problems.
- Medtronic recently announced positive pivotal clinical data for CryoCath's Arctic Front. CryoCath had previously sold its surgical cryoablation business to ATS Medical (now being acquired by Medtronic).
- Lead therapeutic products at the time of the IPO which are still in active clinical development are REOLYSIN (OncoLytics Biotech) and Waratah's Islet Neogenesis Therapy, now being developed in a modified form by Transition Therapeutics.

### Product and Corporate Performance of the IPO Class of 1999-2001

Company	Product Performance	Company Status
<b>Financings (\$10 M+)</b>		
Nexia	X	Asset sale; became Enseco Energy Services
CryoCath	P, A	Acquired by Medtronic at premium to market
Neurochem	X, A	Now Bellus Health (BLU); new partner for Kiacta
Chromos	X	Assets acquired by Calyx Bio-Ventures (CYX)
AnorMED	X, P	Acquired by Genzyme at premium to market
ConjuChem	X	Currently in CCAA
GlycoDesign	X	Acquired by Inflazyme for its cash
Ecopia	X, A	Now Thallion (TLN), with 1 active partnered clinical program
ART Advanced Research	X	Assets acquired under CCAA
Cytovax	X	Became Millenium Biologix, which later sold all its assets
Adherex	X	Insufficient funding to run clinicals
<b>Smaller Financings</b>		
Waratah	A	Acquired by Transition Therapeutics
Andromed	P	Assets sold; became Sonomed; assets sold/distributed
Transition Therapeutics	A	Two products in Phase 2 trials
ARIUS Research	A	Acquired by Roche at premium to market
Neptune Technologies	A	Revenues from product sales
Genomics One	X	Became Alert B&C (ACB); seeking strategic alternatives
OncoLytics Biotech	A	Lead product starting Phase 3
BioMax	X	Assets sold
<b>RTOs</b>		
BioMS	X, A	Invested in Spectral Diagnostics for Toraymyxin
Bioxel	X	Sold assets under CCAA
Medicure	X	In survival mode after Phase 3 failure
MedMira	P	Revenues from diagnostic product sales
Pheromone Sciences	X, A	Acquired new technologies; now Sernova (SVA)
<i>Product Performance: P = Product Approved; A = Active Development; X = Development Problems</i>		
<i>Source: Company reports and regulatory filings</i>		

Share price performance is the more important performance assessment from the perspective of investors.

- Double in two years after IPO – achievement of a post-IPO double within two years would be dependent upon general market and sector performance in addition to the company and product progression. Timing is important - AnorMED achieved the double partially because the IPO happened one year prior to the market peak. Oncolytics Biotech achieved its post-IPO double, actually reaching \$20 from an IPO price of \$0.85, partially because of timing but also partially because the IPO was priced to appeal to the retail investor. Other smaller financings and RTOs were also generally priced to appeal to the retail investor.
- Trading opportunities – share price volatility, caused by company events, general market or sector trends, results in trading opportunities for investors. Since it has been ten years since the middle of the 1999-2001 biotech boom, investors would have expected several trading opportunities. From the IPO class of 24 companies, 14 companies gave investors the opportunity to double their investment at least 3 times during this period.
- Currently trading above the IPO price – only 10 of the 24 companies in the IPO class are still listed and traded, and only Oncolytics Biotech and Neptune Technologies are trading above their IPO prices.

#### Share Price Performance of the IPO Class of 1999-2001

Company	Double Within Two Years After IPO	Three Or More Trading Opportunities	Currently Trading Above IPO Price
<b>Financings (\$10 M+)</b>			
Nexia			n/a
CryoCath		X	n/a
Neurochem		X	
Chromos			n/a
AnorMED	X	X	n/a
ConjuChem		X	n/a
GlycoDesign			n/a
Ecopia		X	
ART Advanced Research			n/a
Cytovax			n/a
Adherex			
<b>Smaller Financings</b>			
Waratah	X	X	n/a
Andromed			n/a
Transition Therapeutics		X	
ARIUS Research		X	n/a
Neptune Technologies		X	X
Genomics One			
Oncolytics Biotech	X	X	X
BioMax			n/a
<b>RTOs</b>			
BioMS		X	
Bioxel	X		n/a
Medicure	X	X	
MedMira	X	X	
Pheromone Sciences	X	X	n/a

Source: Company reports and regulatory filings, TSX Connect

## Performance Summary

We would give the IPO class of 1999-2001 a passing grade on the following basis.

- There have been corporate successes, including three companies acquired at premiums to the market.
- There have been product successes. One therapeutic product has been approved, one medical device has generated clinical data that justifies regulatory approval, several non-therapeutic products are being sold and several therapeutics are still in active clinical development.
- Investors at the time of the IPO could have doubled their money within two years on many of the smaller IPOs and RTOs.
- There were opportunities for trading profits on most of the IPOs, regardless of the size or structure.

## Looking Forward

What is needed to trigger a resurgence of financings and valuations? We believe that the triggers will likely be similar to those for the last boom/window. Stability in the broad market brought some investors back to small and mid cap stocks. Low valuations brought some Canadian investors back into the healthcare sector in 2009. More risk adverse Canadian investors probably need to see some success stories before they will come back to the sector. Success means increased share prices resulting from product approvals, Phase 2 and 3 clinical data, partnerships or companies being acquired.

Only four NCEs (new chemical entities) originating at Canadian biotech companies have previously been approved in the U.S. and E.U.: Photofrin and Visudyne from QLT, Epivir/Lamivudine from BioChem Pharma and Mozobil from AnorMED. The biggest trigger in 2010 could be approval of all three NCEs developed by Canadian companies which are currently under regulatory review: Theratechnologies' tesamorelin (FDA), Cardiome's vernakalant iv (EU) and Lux's LUVENIQ which uses Isotechnika's voclosporin (FDA and EU).

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