



BIOLOGICS COMPANIES IN CANADA

HOW ARE WE FARING?

We in the industry, are all familiar with the stories from ~100 years ago about Canada's global leadership in the discovery of antitoxins and insulin. These discoveries fuelled the growth of Connaught Laboratories, to manufacture biological-based therapeutics to treat serious diseases of the day (e.g. diphtheria, diabetes and later polio). But how has the Canadian biologics industry been faring in the 21st century? Which are the companies that we should be watching out for as the biological-based therapeutics are increasingly becoming the treatment options of choice for the serious diseases of today?

Start with a Baseline – What are Biologics?

The biotechnology industry is confusing at the best of times. Despite our best intentions, we all generally use the terms, biotechnology and biosciences to define what we are all doing, but there are chasms of differences in the scientific research and development activities for which we are each engaged.

Pharmaceutical therapeutics can date back thousands of years, with the ancient

Egyptians using willow trees as a source of acetylsalicylic acid (or aspirin), and purple foxglove flowers as a source of digitalis (or digoxin). The common factor being that these therapeutics are all chemical entities (or small molecules). While many of the original therapeutic compounds were found in nature, the pharmaceutical industry has evolved to reengineer and synthesize their own novel compounds for development as therapeutic candidates.

The best-known story on the first use of a biological-based therapeutic was during the small pox epidemic in the late 18th century. Edward Jenner observed that milkmaids who had been previously exposed to cowpox had built-up an immunity to smallpox. The term “vaccination” originated from infecting individuals with biological material from the cowpox in order for them to build up an immunity to small pox. While vaccines over the past

two centuries have been the most common biological therapeutic, the industry has evolved to include the engineering and biological synthesis of the larger biological molecules, such as novel proteins, antibodies, and nucleotide products. These biological molecules are synthesized in a cellular environment, requiring biological activity to develop them, in contrast to the more traditional chemical synthesis of small molecules.

The past few decades have further complicated the definition of biological therapeutics, with the introduction of genetic engineering, stem cells, and cellular based therapeutics. These are fields in which Canada is well positioned to play a leading role in the development of next generation therapeutics, but these technologies have not been included in the current assessment of Canada's biologics landscape. However, their importance still does warrant further exploration on another occasion.

The focus of this assessment is to review the landscape for Canadian companies that are focused on the development of novel biological-based therapeutics, or biologics.

Global Trends

The pipeline for biologics candidates is growing. A recent Nature Biotechnology article tracked the number of FDA approvals for new drug applications and biological license applications over the past 20 years. Although there have been variations on the total number of approvals from year to year, the average over the first 10 years (1998-2007) showed that 15% of the total 280 application approvals were for biologics, compared to the next 10 years (2008-2017) with 29% of the total 327 approvals for biologics. This trend shows a near doubling of the overall percentage of biological therapeutic candidates versus traditional drug applications.

Statista also recently published data on the number of biologics in development (including preclinical stage). Their data shows that as of June 2017, the number of biologics in development is over 2,700, with the majority of candidates in cancer (at 836), followed by rare diseases (at 566).

These data alone highlight a growing trend for development stage companies focused on biologics, and Canada is home to many companies that are contributing to this global trend.

“With the growing proportion of biologic compounds being developed as therapeutic candidates, it’s important that Canada support companies that are developing this category of therapeutics.”



Profiling Canadian Development Stage Biologic Platform / Therapeutic Companies

An initial search of the Canadian landscape was conducted through the website biopharmaguy.com and supplemented with additional searches of internet resources by the author. The list of companies profiled was selected based on a determination (using public secondary resources) of whether the company was deemed to have IP related to an underlying biologics development platform, or a biologics therapeutic candidate in development. While the assessment of the industry landscape was extensive, it is acknowledged that there may be additional IP based within the Canadian industry landscape that may have been missed through this search process.

A total of 26 Canadian companies were identified and are profiled in Table 1.

Key metrics of note:

- *Regional representation:*

- o Over 50% of companies (15) are located in Western Canada, with the majority (10 companies) in British Columbia and an additional 5 companies in Alberta;

- o Both Ontario and Quebec have a representative number of companies (5 and 4 respectively);
- o Halifax and Moncton are each home to one of the companies.

- *Underlying IP:*

- o Over 50% of the companies (15) have profiled both a proprietary discovery platform as well as internal biologic candidates;
- o An additional 10 companies have profiled therapeutic candidates as their underlying IP and one of the companies has profiled solely their discovery platform as their underlying IP.

- *Development stage and focus:*

- o All 25 companies with therapeutic candidates have ongoing activities at the discovery or preclinical stage of development;
- o At least 14 of the profiled companies have therapeutic candidates in early clinical development;
- o Of the candidates in early clinical development, at least 8 companies (over half of those in clinical development) have focused on cancer.

TABLE 1: Canadian Development Stage Biologic Platform / Therapeutic Companies

Company	Website	Location		Primary Source for Company IP	
		City	Prov	Discovery / Development Platform	Discovery / Development Platform
AbCellera Biologics	www.abcellera.com	Vancouver	BC	Technology for screening and mapping of natural immune responses	
Akshaya Bio	www.akshayabio.com	Edmonton	AB	Chimigen technology platform for developing immunotherapeutic agents and for cell-specific targeted delivery of biologics including siRNA.	Vaccine candidates including: HCV, HBV, HIV at clinical stage; and additional candidates in preclinical development
Alethia Biotherapeutics	www.alethiabio.com	Montreal	QB	Patented discovery platform based on Subtractive Transcription-based Amplification of mRNA (STAR)	Therapeutic candidates for metastatic cancer (pre-clinical) and ovarian & breast cancer (Phase I)
Alpha Cancer Technologies	www.alpha-cancer.com	Toronto	ON	Proprietary recombinant human alpha fetoprotein (AFP) with unique immuno-oncology properties	Lead immunotherapy product in Phase I for multiple indications
Bioasis Technologies	www.bioasis.us	Richmond West	BC	Patented xB3 platform to shuttle neurotherapeutics across the blood brain barrier	In-house development program has preclinical candidates for a few CNS disorders
BriaCell Therapeutics	www.biaccell.com	Vancouver	BC		Clinical stage immunotherapeutics for breast cancer
Cyon Therapeutics	www.cyontherapeutics.com	Vancouver	BC		Antibody candidate for sepsis licensed to Novartis to conduct Phase II trials
	www.feldan.ca	Quebec City	QB	Delivery method for proteins and nucleic acids	Currently developing an antibody program, but no lead therapeutic candidates yet
Feldan Therapeutics	www.formationbiologics.com	Montreal	QB		Four biotherapeutic candidates, with the most advanced ready for Phase II trials
Formation Biologics					
Immunobiochem	www.immunobiochem.com	Toronto	ON	Proprietary technology that enables the development of antibody-drug conjugates (ADCs) targeted at intracellular tumor antigens	Two ADC candidates in preclinical development
ImmunoVaccine	www.imvaccine.com	Halifax	NS	Proprietary DevoVax delivery formulation has applications across multiple therapeutic indications	R&D stage to develop in-house immuno-oncology product candidates
Innovative Targeting Solutions	www.innovativetargeting.com	Vancouver	BC	Patented HuTARG technology platform for protein engineering	Multiple candidates from discovery to pre-clinical development

TABLE 1: Canadian Development Stage Biologic Platform / Therapeutic Companies

Company	Website	Location		Primary Source for Company IP	
		City	Prov	Discovery / Development Platform	Discovery / Development Platform
MedGenesis Therapeutix	www.medgenesis.com	Victoria	BC		Lead candidate for Parkinson's disease just completed Phase II
Northern Biologics	www.northernbiologics.com	Toronto	ON		First in class lead antibody targeting Leukemia Inhibiting Factor ready for Phase I; with other candidates in development
Novelogs Biotechnology	www.novelogs.com	Vancouver	BC	Platform for the discovery and development of monoclonal antibodies that target soluble decoy proteins involved with immune system suppression associated with cancer progression	First in class antibody immunotherapy drug currently focused on multiple myeloma
Oncolytics Biotech	www.oncolyticsbiotech.com	Calgary	AB		A first-in-class intravenously delivered immuno-oncolytic virus (IOV) for the treatment of solid tumors and hematological malignancies
OncoQuest Technologies	www.oncoquestinc.com	Edmonton	AB	Technology platform includes a series of monoclonal antibodies that target several cancer markers	Multiple immuno-therapy candidates in clinical development (Phase I/II)
Parvus Therapeutics	www.parvustherapeutics.ca	Calgary	AB	Navacim platform has the potential to generate multiple unique "First in Class" breakthrough therapeutics for the treatment of autoimmune diseases	Multiple candidates with lead product ready for Phase I
Pascal Biosciences	www.pascalbiosciences.com	Vancouver	BC	Platform to discover and develop targeted agents that enable the body's own immune system to recognize and attack cancers	Product candidates in development
Promedic Life Sciences	www.prometic.com	Laval	QB		Develops both small molecule and plasma derived therapeutics
Quest Pharmatech	www.questpharmatech.com	Edmonton	AB		Majority owner of OncoQuest, which is developing antibody based immunotherapeutic products for cancer
Soricimed Biopharma	www.soricimed.com	Moncton	NB		Developing first in class peptides and peptide-drug conjugates for cancer; lead product completed Phase Ia

TABLE 1: Canadian Development Stage Biologic Platform / Therapeutic Companies

Company	Website	Location		Primary Source for Company IP	
		City	Prov	Discovery / Development Platform	Discovery / Development Platform
Therapten Biosciences	www.therapten.com	Kelowna	BC		Multiple candidates for anticancer protein therapeutics in early development
Turnstone Biologics	www.turnstonebio.com	Ottawa	ON	Engineered biral immunotherapeutic targeting cancer cells	Partnered program in Phase I/II trials, with additional internal programs in pre-clinical development
Vaxil Bio Therapeutics	www.vxlbio.com	Toronto	ON	In-silico platform to identify signal peptides domains and their subsequent use as immunotherapeutic products	Pipeline includes antigen specific immunotherapies and signal peptin specific antibodies, with lead product in Phase I/II
Zymeworks	www.zymeworks.com	Vancouver	BC	Multiple proprietary platforms to support biologics discovery and development	Multiple product candidates for cancer with lead product in Phase I

“While vaccines over the past two centuries have been the most common biological therapeutic, the industry has evolved to include the engineering and biological synthesis of the larger biological molecules, such as novel proteins, antibodies, and nucleotide products.”

Other Key Players in the Canadian Biologics Landscape

Beyond the discovery platforms and therapeutics in development, there are other Canadian companies with valuable biologics IP that are also contributors to the Canadian biologics landscape. The companies focused on the development of biologics products for use as research tools or diagnostic kits are also worth highlighting. While there are many Canadian companies involved in biologics development and marketing (e.g. CRO's and distributors), those we have chosen to highlight are ones that have their own IP related to their novel products or platforms.

An additional 9 companies are highlighted in Table 2. These companies are located in BC, Ontario, and Quebec, and are developers or manufacturers of biological products for health.

It is also important to recognize those companies that are currently marketing biological-based therapeutic products worldwide. Many multinational companies involved in biologics development and marketing have a presence in Canada. These companies bring employment in the sector and more importantly access for Canadians to these novel therapeutics. We celebrate companies like Sanofi Pasteur, which acquired Connaught Laboratories, and has continued to showcase Canada's global leadership in vaccine development and manufacturing for over 100 years.

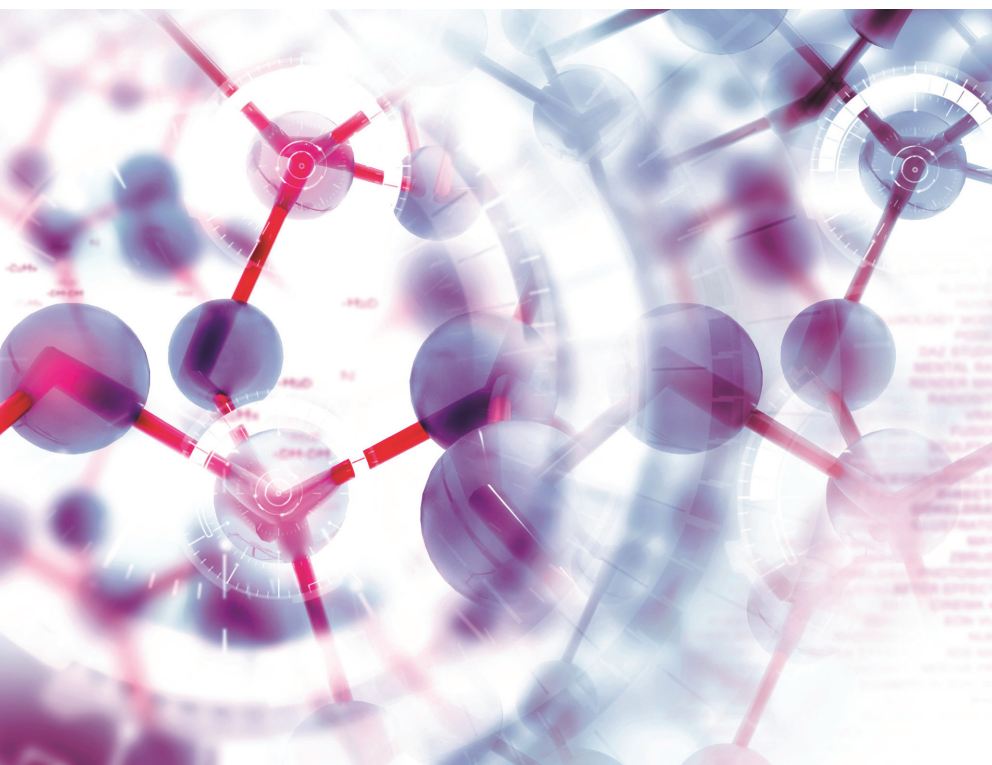
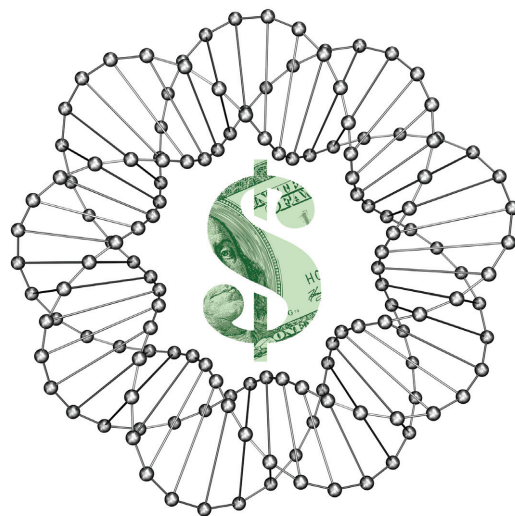


TABLE 2: Canadian Companies Producing Biologics Tools / Kits

Company	Website	Location	
		City	Prov
Affinity Biologicals	www.affinitybiologicals.com	Ancaster	ON
Anogen	www.anogen.com	Mississauga	ON
Augurex	www.augurex.com	Vancouver	BC
Gallus Immunotech	www.gallusimmunotech.com	Mississauga	ON
IgY Life Sciences	www.igylifesciences.com	Toronto	ON
Immune Biosolutions	www.immunebiosolutions.com	Sherbrooke	QB
ImmunoPrecise	www.immunoprecise.com	Victoria	BC
Microbix	www.microbix.com	Mississauga	ON
MRM Proteomics	www.mrmproteomics.com	Montreal	QB



So Why is it Important for Canada to be a Player in the Biologics Sector?

1 Alignment with the global trends – With the growing proportion of biologic compounds being developed as therapeutic candidates, it's important that Canada support companies that are developing this category of therapeutics. Biologics are increasingly becoming recognized for their ability to manage or manipulate biological pathways to achieve a desired outcome. This goes well beyond the ability of chemical compounds to simply turn “on” or “off” certain biochemical functions. The potential for biologic therapeutics has exponentially expanded our ability to treat, manage or even prevent disease.

2 High value products / high value jobs – Biologics as a product are much more complicated to develop, test and manufacture, requiring highly skilled personnel to operate and manage. We have demonstrated a growing number of companies at the development stage, but in order to realize the full economic potential of these companies and novel products, it will be equally important to support the clinical testing and manufacturing capabilities for these companies. Due to the complexity of biologics, they are much more difficult to produce and there is typically an unwillingness to relocate the manufacturing once it has been established. Investment in later

stage development and manufacturing will help to ensure that these companies continue to grow in Canada, providing highly skilled employment, and the global export of high valued products.

3 Novel treatments for improved health – Biologics are opening the door to new options for treatment that were previously unavailable, or perhaps too toxic. Many rare disorders, that previously had few treatment options, are also benefiting from biologics candidates. At the end of the day, treatment of disease is our ultimate goal. If we can continue to support this important sector, then Canadians along with other global citizens will have increased access to novel treatment options for previously untreatable diseases.

Concluding Thought

Canada is recognized as a global player in the biosciences, but it's a hard sell when one of our best stories, that we continue to promote, is the 100-year-old discovery and development of insulin as a novel biologic for diabetes. We need more 21st century success stories to promote and showcase to the global community. The good news, as demonstrated, is that we have a growing pipeline of many more biologics stories to tell. Let's make sure that these companies are supported so that Canada can continue to be recognized as a leading player in novel biologics development.

“Investment in later stage development and manufacturing will help to ensure that these companies continue to grow in Canada, providing highly skilled employment, and the global export of high valued products.”

References:

1. Fresh from the biotech pipeline; Chris Morrison; Nature Biotechnology 36, 131–136 (2018); doi:10.1038/nbt.4068
2. <https://www.statista.com/statistics/258152/biologic-medicines-in-development-by-therapeutic-category-2016/>

Robert Merson is a Certified Management Consultant and entrepreneur in the life sciences sector. He is an occasional contributor to Biotechnology Focus.

▶ To see this story online visit www.biotechnologyfocus.ca/special-report-biologics-companies-in-canada-how-are-we-faring