



Healthcare Industry Update

Thursday, May 31st, 2018



THE ORIGIN RX

Tomato Tomahto

Biologics are becoming gold standard treatments for common conditions such as rheumatoid arthritis, diabetes and certain cancers, offering better outcomes and fewer side effects. The pharmaceutical industry, once dominated by easy-to-manufacture small molecules, is now leaning towards biologics. In fact, biologics represented six of the top eight drugs by revenues. The top-selling drug in the world is Abbvie's Humira, a biologic approved for the treatment of autoimmune diseases like rheumatoid arthritis, psoriasis, and Crohn's, ringing up a whopping US\$16B in revenues.

Case Study. Rituxan (rituximab), a monoclonal antibody, was the first biologic launched commercially. Developed by IDEC Pharma (acquired by Biogen in 2003 for \$6.8B), i.v. Rituxan was initially launched in Switzerland in 1997 and the US the following year, and a more patient-friendly subcu formulation was launched in 2014. It's approved to treat certain cases of non-Hodgkins Lymphoma, rheumatoid arthritis, and organ rejection, with oncology driving the majority of revenue. Sold by Roche, 2017 global sales of Rituxan were over US\$7B.

The manufacturing complexity of biologics involves living microorganisms, plants or animal cells, and often recombinant DNA technology. This makes them very (very!) expensive and is creating enormous demand for generic versions to offset skyrocketing drug costs. Eight cancer treatments approved by the FDA in 2015 had six-figure price tags. In Canada, one course of Rituxan costs approximately \$10,000, with a time interval to re-treatment of 6-12 months.

Biosim competition for Rituxan is available in emerging markets including India, Russia and several countries in Latin America. Sandoz, the Novartis generic subsidiary, received approval for their biosim from the European Medicines Agency (EMA) in June 2017 for all indications of the branded reference product, based on data which confirmed equivalent efficacy, safety, pharmacokinetics and pharmacodynamics. The FDA did not approve applications by Sandoz or Celltrion, but the companies are committed to bringing their biosim to market (Celltrion resubmitted on yesterday's date). Evaluate Pharma predicts Roche's 2022 Rituxan sales will fall to \$2.9B as a result of competition.

The status of biosims. The EMA approved its first biosim in 2006 (somatropin) and a total of 43 to date. The FDA has been slower to allow biosims to market, having approved its first in 2015 (Neupogen) and a total of 10 to date. By the end of this year, it's estimated that biologicals worth more than US\$68B in current annual sales will have lost patent protection. Key players in the biosim market include Sandoz, Teva, Amgen, Apotex, Fuji Pharma, Merck, Celltrion and more.

Before you go and set up your own biosim manufacturing business to participate in this huge market opportunity, let's just say it's not easy. The data required for regulatory approvals together with costly manufacturing processes can easily exceed \$100M. This means that, unlike the market for generic drugs, entrants will likely be compared to the brand, not to each other and biosim competition will be more limited. Also, it looks like uptake of biosimilars requires lots of positive data to boost confidence and encourage substitution, as demonstrated by market entrants to date. Payers/reimbursement will play a key role in biosim adoption, the same way they do to encourage generic usage. Taking all these costs together, price discounts on biosims are not likely to be extremely juicy, but savings of 20%-30% will represent meaningful dollars.

CATHY STEINER, PRINCIPAL





BIGGEST MOVERS

Recent News¹

Markets have been picking up in the second half of May, with the TSX increasing 4.4% and the Nasdaq increasing 5.2%. It's been a mixed bag in healthcare subsectors, which follow in this report. Select highlights of the largest share price movers in the healthcare space during the recent period are included below:

- **Minerva Neurosciences** (NASDAQ:NERV, +37%): Minerva is a clinical-stage biopharmaceutical company focused on development of therapies to treat central nervous system disorders. Strong share performance was driven by the results published by The Journal of Clinical Psychiatry, which demonstrated improvements in patients with schizophrenia that were treated with Minerva's roluperidone product
- **Zymeworks Inc.** (TSX: ZYME, +29%): Zymeworks is a clinical-stage biopharmaceutical company developing multifunctional therapeutics. An increase in recent share performance was due to the announcement that it had entered into a new license agreement with Daiichi Sankyo Company, Limited that will give Zymeworks an upfront technology access fee of US\$18 million and the potential to receive up to US\$467 million in potential clinical, regulatory and commercial milestone payments for licenses to Zymeworks' Azymetric and EFACT technology platforms
- **Foundation Medicine** (NASDAQ:FMI, +28%): Foundation Medicine is a molecular information company dedicated to a transformation in cancer care. The rise in recent share performance was driven by the announcement that the Centers for Medicare & Medicaid Services (CMS) approved new Advanced Diagnostic Laboratory Test (ADLT) status for FoundationOne CDx, which is the first FDA-approved comprehensive genomic profiling assay for all solid tumors. This means that for the nine-month period beginning on July 1st CMS will provide reimbursement for covered FoundationOne CDx tests at the rate of US\$3,500.
- **TransEnterix, Inc** (NYSE:TRXC, +28%): TransEnterix is a medical device company that improves minimally invasive surgery by digitizing the interface between the surgeon and the patient. Strong recent share performance was due to the announcement that it had received FDA 510(k) clearance for expanded indications of its Senhance Surgical System product, which has more than doubled its total addressable annual procedures to over three million
- **Recro Pharmaceutical** (Nasdaq:REPH, -50%): Recro Pharmaceutical is a specialty pharmaceutical company focused on therapeutics for the hospital and other acute care settings. The decline in recent share price was driven by an announcement that the FDA was unable to approve the New Drug Application for IV meloxicam
- **Jounce Therapeutics, Inc.** (NASDAQ:JNCE -34%): Jounce Therapeutics is a clinical-stage immunotherapy company that focuses on discovery and development of therapies for the treatments of cancer. Recent poor share performance has been driven by inconclusive results from the preliminary American Society of Clinical Oncology data for its drug JTX-2011, which is intended to be a treatment for various solid tumour cancers

Note 1: For the period May 16th to May 31st, 2018

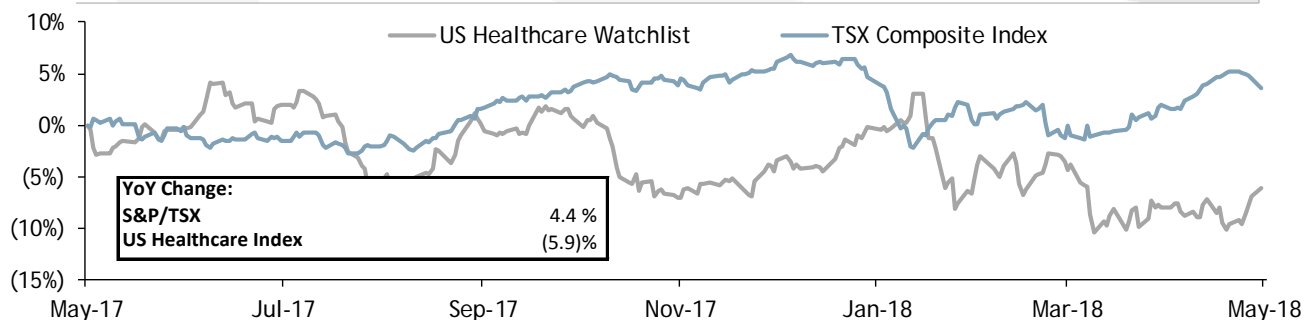


US HEALTHCARE WATCHLIST

News Scan¹

- The US Healthcare Watchlist index lost approximately 5.9% over the last twelve months, while the TSX Composite Index gained 4.4% over the same period. Some events making news recently:
- On May 31st, **Allergan Plc.**, a multinational drugmaker based in Ireland, announced its plans to sell two of its smaller businesses, the women's health and infectious disease units, in efforts to reduce recent share price pressure. Following the divestiture, the company plans to focus on its four core businesses: medical, aesthetics, central nervous system, eye care and gastrointestinal products
- On May 24th, **Novartis AG**, a global healthcare company based in Switzerland, received approval from the European Commission for Zessly, a treatment for gastroenterological, rheumatological, and dermatological diseases
- On May 17th, **Novartis AG**, also received FDA-approval of Aimovig, a novel treatment developed specifically for migraine prevention. It is the first and only FDA-approved treatment to block the calcitonin gene-related peptide receptor (CGRP-R), a key contributor in migraine
- On May 15th, **Novartis AG**, announced its completed acquisition of **AveXis Inc.**, a clinical-stage gene therapy biotech company, through the consummation of a merger of its indirect wholly-owned subsidiary, **Novartis AM**. In the merger, each share of AveXis has the rights to receive US\$218.0 per share. Following the acquisition, **Novartis** plans to integrate **AveXis'** leading gene therapy technology to develop the first one-time gene-based treatment for spinal muscular atrophy for children
- On May 24th, **Johnson & Johnson**, a diversified multinational healthcare and consumer company, was dealt a US\$25.8 million lawsuit verdict in its talc-asbestos case by a California jury, stating the company among other companies were negligent and did not warn consumers of possible health risks from its Baby Powder
- On May 23rd, **Pfizer Inc.**, a pharmaceutical conglomerate, announced that tafamidis, an investigational treatment for transthyretin cardiomyopathy, a rare, fatal, and underdiagnosed condition associated with progress heart failure, received a Breakthrough Therapy designation from the FDA
- On May 23th, **Pfizer Inc.**, recalled over 1.8 million vials of piperacillin and tazobactam, products used to treat different infections caused by bacteria. According to the FDA, the products were manufactured by Hospira Healthcare India Private Ltd. to be sold in the U.S. It was reported that the products contained elevated levels of impurities that may result in decreased potency
- On May 22nd, **Pfizer Inc.** announced that it has started a Phase 1/2 trial of its respiratory syncytial virus (RSV) vaccine candidate in health adult volunteers
- On May 21st, **GlaxoSmithKline PLC.**, a pharmaceutical company based in London, received approval from the FDA for Arnuity Ellipta, a once-daily inhaled corticosteroid (ICS) medicine for the maintenance treatment of asthma in children

Relative Performance Index



Note 1: For the period May 16th to May 31st, 2018

US Healthcare Watchlist Constituents: Johnson & Johnson, Pfizer Inc., Roche Holding AG, Novartis AG, Merck & Co., Inc., AbbVie Inc., Amgen Inc., Medtronic plc, Gilead Sciences, Inc., Bayer AG, Abbott Laboratories, Bristol-Myers Squibb, GlaxoSmithKline plc, Eli Lilly and Company, AstraZeneca PLC, Celgene Corporation, Allergan plc, Boston Scientific Corporation, Mylan N.V., Teva Pharmaceutical Industries, Mallinckrodt Public Limited Company, Endo International plc

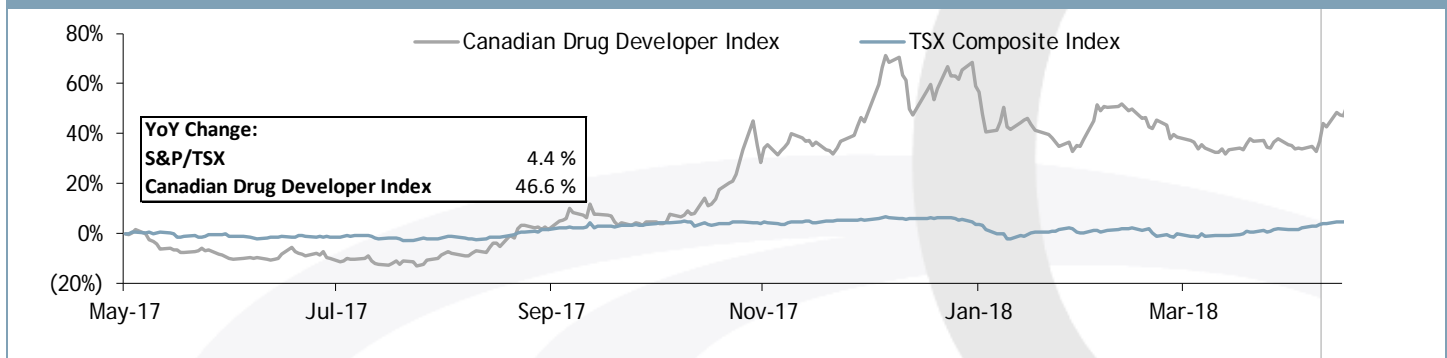


CANADIAN DRUG DEVELOPERS

News Scan¹

- The Canadian Drug Developers Index gained approximately 46.6% over the last twelve months, while the TSX Composite Index gained 4.4% over the same period. Some events making news this month:
- On May 17th, **Oncolytics Biotech Inc.**, a biotechnology company that discovers and develops pharmaceutical products for the treatment of cancers, announced a collaboration with **Merck Inc.** and **Northwestern University** in a phase 2 second line pancreatic cancer study. The study plans to enroll approximately 40 patients with advanced pancreatic cancer
- On May 14th, **InMed Pharmaceuticals Inc.**, a pre-clinical stage biopharmaceutical company that develops therapeutics using cannabinoids coupled with innovative drug delivery systems, announced that it had filed a patent application for INM-085 glaucoma program. The drug is intended for application as a once-per-day eye drop intended to assist in reducing the high rate of non-adherence with current glaucoma therapies
- On May 14th, **Zymeworks Inc.**, is a clinical-stage biopharmaceutical company developing multifunctional therapeutics, announced that it had entered into a new license agreement with **Daiichi Sankyo Company, Limited**. This new license agreement allows Daiichi to acquire licenses to Zymeworks' Azymetric and EFECT technology platforms to develop two additional bispecific antibody therapeutics. Zymeworks received an upfront technology access fee of US\$18 million and has the potential to receive up to US\$466.7 million in potential clinical, regulatory and commercial milestone payments

Relative Performance Index



Note 1: For the period May 15th to May 31st, 2018

Canadian Drug Developers Constituents: ProMetic Life Sciences Inc., Clementia Pharmaceuticals Inc., Aurinia, Pharmaceuticals Inc., Arbutus Biopharma Corporation, Resverlogix Corp., Aquinox Pharmaceuticals, Inc., Zymeworks Inc., ImmunoVaccine Inc., InMed Pharmaceuticals Inc., Sierra Oncology, Inc., Tetra Bio-Pharma Inc., Oncolytics Biotech Inc., Cardiome Pharma Corp., ProMIS Neurosciences Inc., Aeterna Zentaris Inc., Trillium Therapeutics Inc.

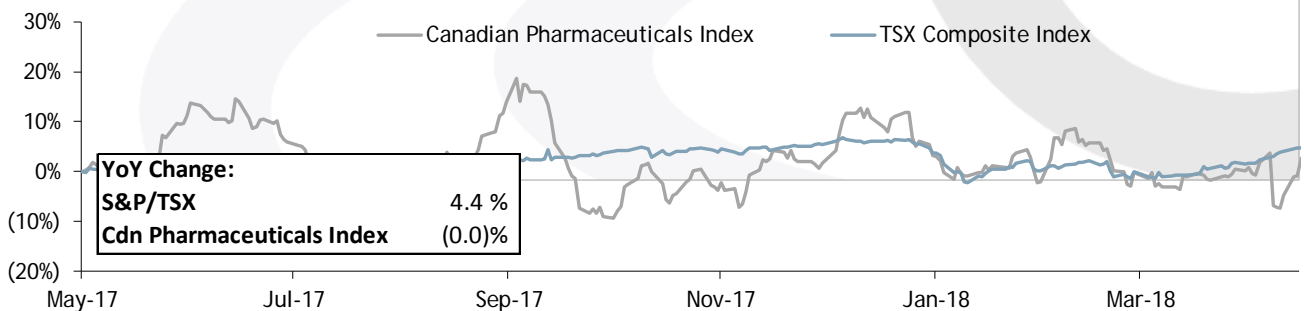


CANADIAN PHARMACEUTICALS

News Scan¹

- The Canadian Pharmaceuticals Index broke even at about 0.0% over the last twelve months, while the TSX Composite Index gained 4.4% over the same period. Some events making news this month:
- On May 30th, **Theratechnologies Inc.**, a specialty pharmaceutical company focusing on healthy aging and improved quality of life among HIV patients, announced that it reached an agreement with **EMD Serono Inc.**, to immediately pay all outstanding obligations related to the repurchase of the commercial rights to EGRIFTA at a renegotiated price. The amended agreement allows Theratechnologies to make a lump sum payment of US\$23.85 million instead of royalties that would have been payable over the next four to five years
- On May 30th, **HLS Therapeutics Inc.**, a specialty pharmaceutical company focused on the acquisition and commercialization of branded pharmaceutical products, announced that it had entered into an automatic share purchase plan with a designated broker. This was done in order to facilitate repurchases of its common shares under its previously announced normal course issuer bid
- On May 29th, **Acerus**, a pharmaceutical company that develops women and men's health products, announced that it had entered into an exclusive agreement to acquire **Pharmanest AB's** short acting lidocaine product, a novel pain relief drug device combination for gynecological procedures in Canada. The product was acquired to help broaden Acerus' women's health product portfolio
- On May 17th, **Acerus** also reported that it entered into an agreement with **Mattern Pharma AG** to buy out all of its obligations under their license agreement, including
- On May 17th, **Valeant Pharmaceuticals International Inc.**, a global company that develops, manufactures and markets a range of pharmaceuticals, medical devices and over-the-counter products, announced it has priced its previously announced offering of C\$750,000,000 aggregate principal amount of 8.50% unsecured senior notes due 2027. The offering is expected to close around June 1, 2018
- On May 15th, **Cipher Pharmaceuticals Inc.**, a growing specialty pharmaceutical company focused on dermatology, announced it has completed a 100% acquisition of **Cardiome Pharma Corp.** for C\$25.5 million in cash consideration. The purpose of the acquisition was to enable Cipher to acquire the Canadian business portfolio of Cardiome by way of the acquisition of all of the issued and outstanding common shares

Relative Performance Index



Note 1: For the period May 16th to May 31st, 2018

Canadian Pharmaceuticals Constituents: Valeant Pharmaceuticals International, Inc., Knight Therapeutics Inc., Concordia International Corp., Aralez Pharmaceuticals Inc., Theratechnologies Inc., Zomedica Pharmaceuticals Corp.,

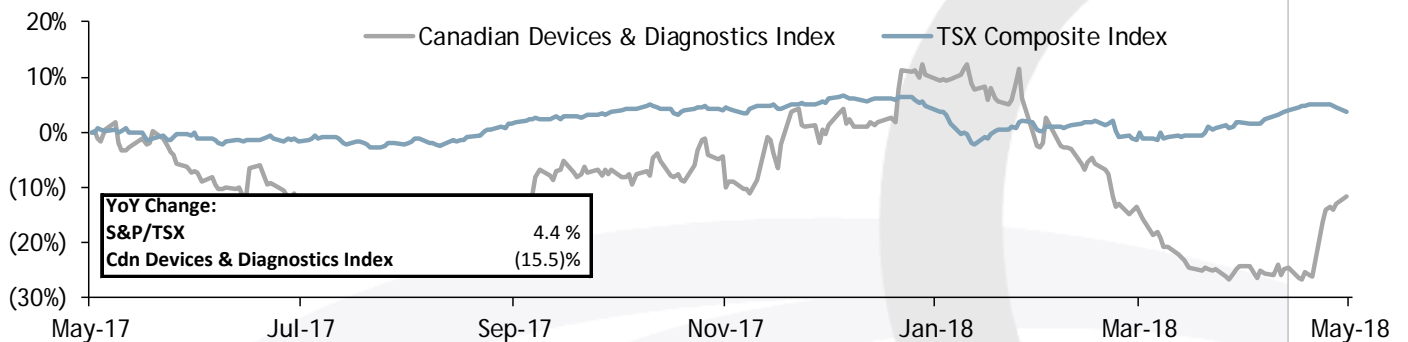


CANADIAN DEVICES & DIAGNOSTICS

News Scan¹

- The Canadian Devices & Diagnostics index lost approximately 15.5% over the last twelve months, lagging the TSX Composite Index which gained 4.4% over the same period. Newsmakers for the last two weeks of May 2018:
- On May 24th, **ChroMedX Corp.**, a developer of the HemoPalm Handheld Blood Analyzer platform, announced the closed acquisition of **UX Data Sciences Corp.**, an Ontario-based medtech data science company for an undisclosed amount. The acquisition will provide **ChroMedX** benefits from **UX Data Sciences'** partnership with IBM's Incubator Project and working capital, including approximately \$500,000 in cash, for continued development of the UXD system
- On May 17th, **Canary Medical Inc.**, a medical data company dedicated to improved healthcare outcomes through the improved use of proprietary, smart medical devices, received a US\$10 million investment from **Quark Venture Inc.** and **GF Securities**, through their Global Health Sciences Fund (GHS). The Canary Health Implantable Reporting Processor (CHIRP) uses innovative sensor and novel communication technology in medical devices to enable remote patient monitoring and self-reporting without the need for physician intervention or a dependence upon patient compliance

Relative Performance Index



Note 1: For the period May 16th to May 31st, 2018

Canadian Devices and Diagnostics Constituents: CRH Medical Corporation, TSO3 Inc., Titan Medical Inc., Opsens Inc., Neovasc Inc., ChroMedX Corp., Profound Medical Corp., Covalon Technologies Ltd., Spectral Medical Inc., Hamilton Thorne Ltd.

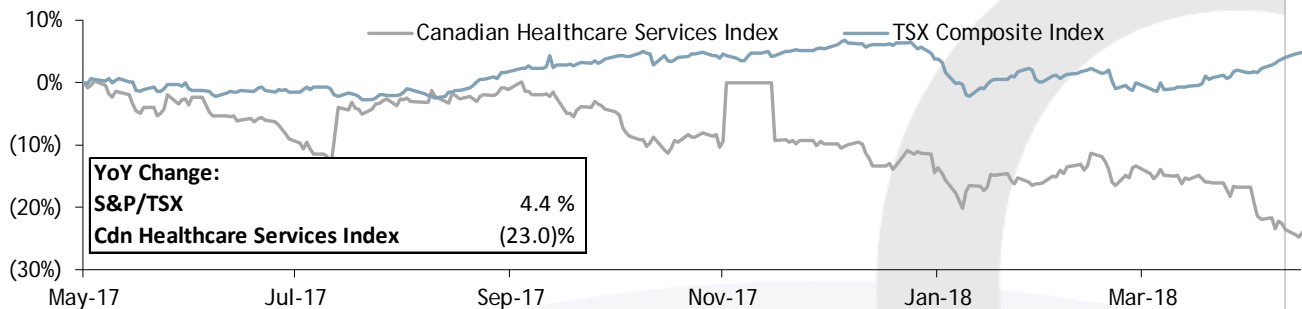


CANADIAN HEALTHCARE SERVICES

News Scan¹

- Last twelve-month performance of the Canadian Healthcare Services index decreased 23.0%, while the TSX Composite Index increased 4.4% over the same period. Some events making news this period include:
- On May 24th, **Akrium Inc.**, a leading provider of outpatient diagnostic imaging services, announced that its wholly owned subsidiary **Preferred Medical Imaging, LLC** had closed its previously announced US\$21.6 million non-controlling acquisition in seven of its existing Texas-based diagnostic imaging centers
- On May 14th, **Medical Facilities Corporation**, a company that owns surgical facilities in the United States that deliver innovative high-quality medical care, announced that that the **Toronto Stock Exchange** had approved its notice of intent to make a normal course issuer bid for 2% of its common shares issued and outstanding as of May 2nd at an average price of C\$14.71.

Relative Performance Index



Note 1: For the period May 16th to May 31st, 2018

Canadian Healthcare Services Constituents: *Sienna Senior Living Inc., Extencicare Inc., Medical Facilities Corporation, Akumin Inc, Centric Health Corporation*

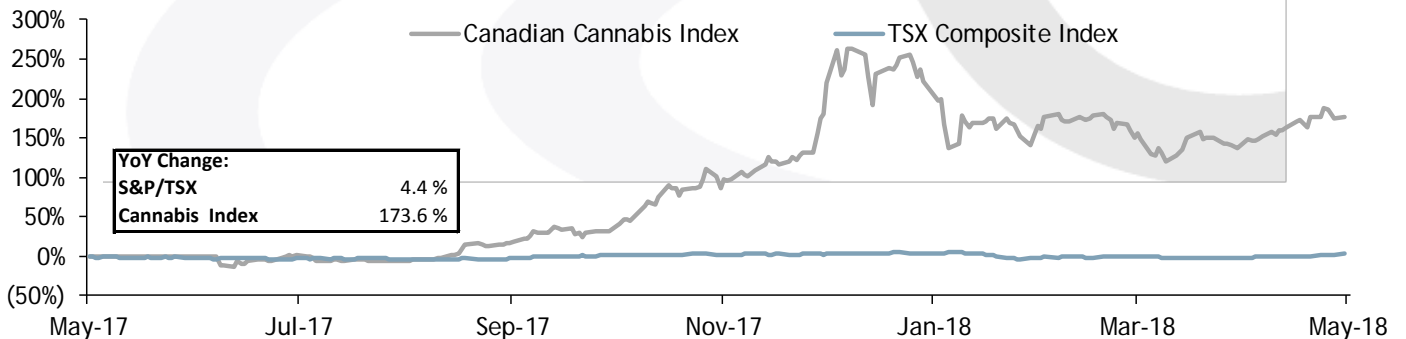


CANNABIS

News Scan¹

- Last twelve-month performance of the Cannabis index was approximately 173.6% dwarfing the 4.4% gain of the TSX Composite Index over the same period. Highlights of cannabis news for the last two weeks of May 2018:
- On May 31st, **Aphria Inc.**, a Canadian medical cannabis company, announced that it has entered into a series of agreements resulting in forming a joint venture, **CannInvest Africa Ltd.**, with South African company **Verve Group of Companies**. As part of this transaction, **CannInvest** will acquire an interest in **Verve Dynamics Inc.**, a licensed producer of medical cannabis extracts in Lesotho, for C\$4.1 million
- On May 30th, **Canopy Growth Corp.**, a medical marijuana company based in Ontario, announced its acquisition of **Daddy Cann Lesotho PTY Ltd.**, a licensed producer and distributor of marijuana in Lesotho, Africa. This acquisition will enable both companies to achieve low operating and resource costs in ideal humidity and growing condition for greenhouse cultivation in Africa. **Daddy Cann Lesotho** is also well-positioned to penetrate the South African market
- On May 28th, **Tetra Bio-Pharma Inc.**, a biopharmaceutical leader in cannabinoid-based drug discovery and development, announced that it had backed **North Bud Farms Inc.** to list on the Canadian Securities Exchange. Tetra plans to distribute 15,000,000 common shares to its shareholders as a pro rata dividend, concurrently with the listing of North Bud Farms common shares on the CSE
- On May 24th, **Organigram Holdings Inc.**, a licensed producer of marijuana based in New Brunswick, announced that it has entered into a letter of intent with **Hyasynth Biologicals Inc.** for a proposed strategic alliance, in which Organigram can purchase a pre-defined quantity of a range of cannabinoids or cannabinoid-related production from Hyasynth on certain terms
- On May 21st, **Canada's Island Garden**, Prince Edward Island's only federally licensed producer of cannabis, received a C\$27.0 million investment from **Alliance Once International Inc.**, its parent company, to significantly increase its cannabis production growth and to support the launch of a new brand
- On May 16th, **Maricann Group Inc.**, a producer and distributor of medical cannabis, announced that it has entered into a non-binding LOI to acquire **Medican Holdings Ltd.** of the Republic of Malta. **Medican's** subsidiary, **Medican Research Group**, is a licensed producer of cannabis in Malta, and the license will give **Maricann** the ability to import, extract, manufacture finished products, and distribute medical cannabis within Malta and the European Union

Relative Performance Index



Note 1: For the period May 16th to May 31st, 2018

Cannabis Index Constituents: Canopy Growth Corporation, Aurora Cannabis Inc., Aphria Inc., MedReleaf Corp., CannTrust Holdings Inc., CanniMed Therapeutics Inc., Cannabis Wheaton Income Corp., OrganiGram Holdings Inc., The Supreme Cannabis Company, Inc., The Hydrothecary Corporation



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