

Healthcare Industry Update

Wednesday, August 15th, 2018



THE ORIGIN RX

Price is what you pay. Value is what you get. (Warren Buffett)

We are following up with progress by GW Pharmaceuticals, whose Epidiolex is the first FDA-approved cannabis-based medication. We've been waiting on guidance from GW regarding pricing, and last week they said a course of their proprietary oral solution of pure plant-derived CBD will cost \$32,500 annually. For a quick recap: Epidiolex received its breakthrough approval by the FDA a couple of months ago for the treatment of two rare forms of epilepsy, Lennox-Gastaut syndrome (LGS) and Dravet syndrome. It is currently scheduled as a drug with "no currently accepted medical use", but the DEA has 90 days from the June 25 approval to reschedule it, so it's about a month away.

If you have sticker shock after hearing the price, let's try to put it into the context offered by GW. The price is said to be in line with other branded antiepileptic medicines as well as feedback from insurance companies. It is at the low end of analysts' price forecasts, which were in the range of \$30,000 to \$60,000 a year. Moreover, Epidiolex is pharmacy-grade and has gone through the rigour of clinical trials, showing statistically significant reduction in the frequency of seizures compared to placebo in three randomized, double-blind, placebo-controlled clinical trials involving 516 patients.

But at the other end of the scale is CBD purchased online or at a dispensary. Should we look at the dispensary product like a sortof, kind-of generic? In the pharma world, generics have to show bioequivalence. But not so in the cannabis world. Dispensary CBD isn't likely to be a pharma-grade dose with clinically demonstrated efficacy or bioavailability. Having said that, there are medical cannabis providers who are carrying out placebo-controlled trials. These trials may not be as large as GW's, but they are likely to be a cost-effective basis for demonstrating an effective product and a good whitepaper strategy.

GW argues the co-pay for Epidiolex, for those patients with insurance, should run less than dispensary CBD. This means the blockbuster potential of Epidiolex will be closely tied to its insurance coverage. That's no different than usual, but in this case there will be a "generic" product readily available at the same time as the branded one. The clinical rigour and FDA approval, together with the lack of treatment options for children with these rare diseases are expected to result in insurance coverage for the drug. Stay tuned.

CATHY STEINER, PRINCIPAL







BIGGEST MOVERS

Recent News¹

Markets have been relatively flat in the last two weeks with the TSX decreasing 0.5% and the NASDAQ increasing by 0.9%. It's been a mixed bag in healthcare subsectors, which follow in this report. A selection of the largest share price movers in the healthcare space during the recent period is included below:

- <u>Strongbridge Biopharma plc</u> (NasdaqGS:SBBP +26%): Strongbridge Biopharma is a commercial-stage pharmaceutical company focused on the development and commercialization of therapies for rare diseases. Recent share price appreciation was due to an announcement of positive top-line results from the pivotal Phase 3 SONICS study evaluating RECORLEV (levoketoconazole) for the treatment of endogenous Cushing's syndrome
- <u>Antares Pharma, Inc.</u> (NasdaqCM:ATRS +23%): Antares Pharma is a specialty pharmaceutical company focused on the development and commercialization of self-administered parenteral pharmaceutical products using advanced drug delivery auto injection technology. Recent share price increase was mainly due to its announced agreement with <u>Pfizer</u> to develop a combination drug device rescue pen
- Protagonist Therapeutics, Inc. (NasdaqGM:PTGX +20%): Protagonist Therapeutics is a clinical-stage biopharmaceutical company focusing on peptide-based drugs. Strong share price performance was primarily due to its announcement of positive results from the Phase 2 PROPEL study of oral alpha-4-beta-7 integrin antagonist PTG-100 for the treatment of patients with ulcerative colitis (UC)
- <u>BioCryst Pharmaceuticals, Inc.</u> (NasdaqGS:BCRX +17%): BioCryst Pharmaceuticals is a pharmaceutical company focused on the development and commercialization of treatments for rare diseases. The recent increase in its share price was due to the announcement that the <u>FDA</u> has been granted Fast Track designation for its drug, BCX7353, used for the prevention of angioedema attacks in patients with hereditary angioedema (HAE)
- <u>Ovid Therapeutics, Inc.</u> (NasdaqGS:OVID -32%): Ovid Therapeutics is a biopharmaceutical company that develops medicines for patients with neurological disorders. Its recent share price decline was primarily due to doubts from investors about the efficacy of the phase 2 data from a new drug, OV101, used to target Angelman Syndrome. Although the results from the phase 2 trial were positive, investors remain concerned about the effectiveness of the new drug that targets the disease itself when compared to current treatment options that target specific symptoms
- <u>Ampio Pharmaceuticals, Inc.</u> (AMEX:AMPE -85%): Ampio Pharmaceuticals is a clinical-stage biopharmaceutical company primarily focused on the development of therapies to treat prevalent inflammatory conditions. Share prices declined significantly after the <u>FDA</u> rejected Ampio's Biologics License Application (BLA) for its drug, Ampion, aimed at treating osteoarthritis of the knee

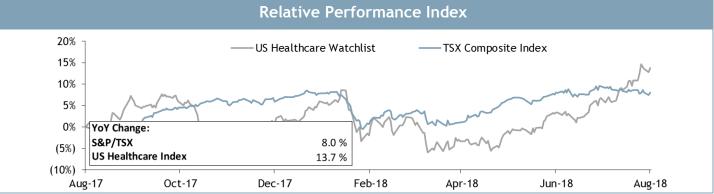
Note 1: For the period August 2nd to August 15th, 2018



US HEALTHCARE WATCHLIST

News Scan¹

- The US Healthcare Watchlist Index gained approximately 13.7% over the last twelve months, while the TSX Composite Index gained 8.0% over the same period. Some events making news this month:
- On August 15th, <u>Oscar Health</u>, a technology-focused health insurance company, announced that <u>Alphabet Inc</u> plans to invest US\$375 million in its company to help it expand to more markets and business segments including Medicare Advantage in 2020. This investment comes months after Oscar Health raised US\$165 million in a funding round. Following the completion of the investment, Alphabet will own approximately 10% of Oscar
- On August 15th, <u>Endo International</u>, a generics and specialty branded pharmaceutical company, announced that it is lifting a temporary stay of its litigation against the <u>US FDA</u>. The litigation filed in October 2017 seeks a declaration that the FDA's Interim Policy on compounding using bulk drug substances is contrary to law because it authorizes bulk compounding of new drugs where the applicable DQSA requirements are not satisfied. It also seeks the removal of vasopressin from FDA's Category 1 list to assure that outsourcing facilities don't engage in bulk compounding of vasopressin-containing drug products
- On August 13th, <u>Bayer's Monsanto</u>, an agrochemical and agricultural biotechnology company, announced that the US federal court in California ruled for the company to pay US\$289 million in damages for the linkage of cancer to their "Round-Up" products. Following the announcement, <u>Bayer's</u> shares plunged 14% amounting to approximately US\$14 billion in value
- On August 9th, <u>Rite Aid</u>, an American drugstore chain, and <u>Albertsons</u>, an American grocery company, canceled their planned US\$24 billion merger due to mounting shareholder opposition regarding value expectations
- On August 8th, <u>Boston Scientific</u>, a US manufacturer of medical devices used in interventional medical specialties, announced it entered into an agreement to acquire <u>Veniti</u> for US\$108 million in cash, a California based medical device company that treats venous obstructive diseases. Boston Scientific currently hold a 25% stake in the company and faces a \$52 million payment contingent on <u>FDA</u> approval for the self-expanding VICI stent system
- On August 6th, <u>Teva Pharmaceuticals</u>, a multinational pharmaceutical company, received <u>FDA</u> approval for GRANIX in an injection format of 300mcg/1ml and 480mcg/1.6ml single-dose vials, which treats severe neutropenia in adults and in pediatric patients 1 month and older. Prefilled syringes of GRANIX will be available in the US shortly
- On August 6th, <u>Gilead Science</u>, an American biopharmaceutical company, announced that the <u>China National Drug</u>
 <u>Administration</u> approved Genvoya, a single tablet regiment that treats HIV for adolescents 12 years and older. The drug will soon be accessible to thousands of Chinese citizens
- On August 6th, <u>Antares Pharma</u>, a developer of parenteral therapeutic products, announced it entered into an agreement with <u>Pfizer</u>, an American pharmaceutical company, to develop a combination drug device rescue pen that includes an undisclosed Pfizer drug. Pfizer has agreed to pay for the development and in obtaining FDA approval for the product
- On August 2nd, global drugmaker <u>Eli Lilly's Elanco Animal Health</u> division filed for an IPO with US regulators to list on the NYSE with the proposed IPO size of up to US\$100 million. Lilly is expected to own less than 20% of the new company



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<u>US Healthcare Watchlist Constituents</u>: 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

- Last twelve-month performance of the Canadian Drug Developers Index was an impressive 49.0%, significantly outperforming the TSX Composite Index which only gained 8.0% over the same period. In the news this month:
- On August 14th, <u>Correvio Pharma Corp.</u>, a specialty pharmaceutical company based in Vancouver, announced that Brinavess, its antiarrhythmic drug for rapid conversion of recent onset atrial fibrillation, was selected by the <u>China FDA</u> as potentially eligible for priority review. Brinavess was one of 48 therapies assessed as "clinically urgently needed new drugs"
- On August 14th, <u>Arbutus Biopharma Corporation</u>, a Hepatitis B Virus (HBV) therapeutic solutions company, announced its lipid nanoparticle licensee, <u>Alnylam Pharmaceuticals</u>, announced that their new drug application for ONPATTRO, an RNAi therapeutic, received approval by the <u>US FDA</u>. The drug treats hereditary ATTR amyloidosis with polyneuropathy and it is the first RNA interference therapeutic product approved by the FDA
- On August 13th, <u>Medicure Inc</u>, a cardiovascular pharmaceutical company, announced that the <u>US FDA</u> approved its Abbreviated New Drug Application for Sodium Nitroprusside Injection single dose vial (SNP), a generic intravenous cardiovascular drug product. SNP is indicated for the immediate reduction of blood pressure for adults and pediatric patients in hypertensive crisis
- On August 9th, <u>Tetra Bio-Pharma</u>, a developer of cannabinoid-based drugs, announced that <u>Health Canada</u> approved its protocol for a clinical trial investigating its PPP001 drugs as an alternative to the opioid fentanyl in the management of breakthrough cancer pain. The trial will assess the time-to-relief in patients suffering from breakthrough cancer pain. Based on its clinical data, the company believes that the pharmacodynamic properties of PPP001 may provide a novel faster acting alternative to the opioid fentanyl
- On August 7th, <u>Prometic Life Sciences</u>, a global biopharmaceutical company, announced that the <u>US FDA</u> granted a Rare Pediatric Disease Designation to its small molecule drug candidate, PBI-4050, for the treatment of Alström syndrome
- On August 7th, <u>Hoffmann-La Roche Canada</u>, a subsidiary of a multinational healthcare company, announced that <u>Health</u> <u>Canada</u> approved HEMLIBRA (emicizumab injection) for hemophilia A patients with factor VIII inhibitors as routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes. In two of the largest clinical studies, HEMLIBRA substantially reduced bleeding in adults and children compared to prior episodic treatment with bypassing agents
- On August 7th, <u>Resverlogix Corporation</u>, a developer of apabetalone, announced that the <u>Independent Data and Safety</u> <u>Monitoring Board (DSMB)</u> for the Company's Phase 3 BETonMACE trial in high-risk cardiovascular disease (CVD) patients, completed a seventh planned safety review and recommended that the study should continue as planned without any modifications

Relative Performance Index							
120% - 100% - 80% - 60% - 40% - 20% -	YoY Change: S&P/TSX Canadian Dru	g Developer Index	Canadian Drug 8.0 % 49.0 %	Developer Index	— TSX Compo	osite Index	~~~
0% - (20%) -					~~~~~		
()	g-17	Oct-17	Dec-17	Feb-18	Apr-18	Jun-18	Aug-18

Note 1: For the period August 2nd to August 15th, 2018

<u>Canadian Drug Developers Constituents</u>: 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., Acerus Pharmaceuticals Corporation, ProMIS Neurosciences Inc., Aeterna Zentaris Inc., Trillium Therapeutics Inc.



CANADIAN PHARMACEUTICALS

News Scan¹

- The Canadian Pharmaceuticals Index experienced a decline of approximately 11.9% over the last twelve months, while the TSX Composite Index gained 8.0% over the same period. Recent news highlights include:
- On August 13th, <u>Concordia International Corp.</u>, an international specialty pharmaceutical company, announced that in connection with its previously announced recapitalization transaction, it intends to complete a non-brokered private placement for the amount of US\$1.16 million. Management will subscribe for up to 85,000 limited voting shares at an issue price of US\$13.69 per share
- On August 10th, <u>Nuvo Pharmaceuticals</u>, a global pharmaceutical company based in Mississauga, announced the signing of a letter of intent with <u>Aralez Pharmaceuticals</u>, a specialty pharmaceutical company. Nuvo agreed to acquire a portfolio of more than 20 revenue-generating products, as well as the associated personnel and infrastructure, for US\$110 million in cash. The acquisition also includes Aralez's Canadian specialty pharmaceutical business, which offers Cambia, Blexten, Suvexx, the Canadian distribution rights to Resultz, and other worldwide rights
- On August 9th, <u>Pivot Pharmaceuticals</u>, a Canadian biopharmaceutical company, announced the signing of a letter of intent for the supply of cannabis oils and isolates with <u>Pharmaflorx Ltd</u>, a privately-held late-stage Access to Cannabis for Medical Purposes Regulations (ACMPR) applicant located in Quebec. Pivot will purchase a minimum of 1,000 kg/year of cannabis oils and isolates for the manufacturing of Pivot's patented portfolio of biocannabis products
 - On August 8th, <u>Pivot Pharmaceuticals'</u> subsidiary, <u>Pivot Naturals</u>, entered into a binding letter of intent with <u>Healthcare Options for Patient Enterprises (HOPE)</u>, a fully licensed extractor, manufacturer, and distributor of cannabis products based in Las Vegas, Nevada. The agreement will be completed sometime in August, and will include a non-exclusive grant of license to HOPE to commercialize Pivot's cannabis powder technology in Nevada, distribution rights to sell each other's products, and rights to manufacture each other's products. Pivot is set to enter the Nevada cannabis market with this strategic partnership
- On August 3rd, <u>Bausch Health Companies'</u> subsidiary, <u>Salix Pharmaceuticals</u>, a specialty pharmaceutical company focused on the treatment of gastrointestinal (GI) disorders, announced it entered into a research agreement with <u>Cedars-Sinai</u> <u>Medical Center</u> to investigate the microbiome in the treatment of GI disorders

Relative Performance Index



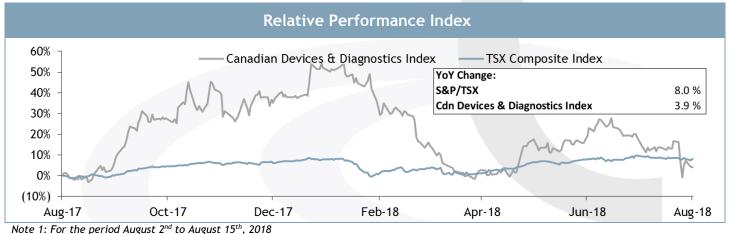
Canadian Pharmaceuticals Constituents: Bausch Health Companies Inc., Knight Therapeutics Inc., Concordia International Corp., Aralez Pharmaceuticals Inc., Theratechnologies Inc., Zomedica Pharmaceuticals Corp.



CANADIAN DEVICES & DIAGNOSTICS

News Scan¹

- The Canadian Devices & Diagnostics Index lost approximately 3.9% over the last twelve months, lagging the TSX Composite Index which gained 8.0% over the same period. Newsmakers for August 2018:
- On August 15th, <u>GeneNews Limited</u>, an innovator in the liquid biopsy space, announced a partnership with <u>LifeX</u>, a developer of solutions to alleviate suffering and death from intractable diseases. Together, both will develop strategies for incorporating several proprietary, early cancer diagnostics into healthcare settings to improve patient compliance with cancer screening
- On August 14th, <u>MolecuLight Inc.</u>, a Canadian medical imaging company, received <u>FDA</u> clearance for US market sales for its fluorescence imaging device, the MolecuLight i:X. The device digitally captures and documents fluorescence information from wounds and surrounding tissue using still images and videos in real-time
- On August 6th, <u>Sotera Health LLC</u>, a provider of microbiological and analytical laboratory tests for the medical device industry, announced the closing the sale of its Medical Isotopes segment to <u>BWX Technologies</u>. With the sale, BWX now owns Nordion's former medical isotopes business, including the radiochemical and contract manufacturing operations
- On August 3rd, <u>Neovasc Inc.</u>, a developer of minimally invasive transcatheter mitral valve replacement technologies, announced that it has entered into a collaboration and licensing agreement with <u>Penn Medicine</u> and the <u>Gorman</u> <u>Cardiovascular Research Group</u>. The four-year agreement contains essential Penn Medicine, which will help Neovasc safeguard their efforts to further develop and commercialize Tiara, their minimally invasive transcatheter device
- On August 2nd, <u>Mindshare Medical</u>, a developer of clinical decision support technology for clinicians and healthcare organizations, announced that its RevealAI-Lung product received approval from <u>Health Canada</u> for use with CT lung cancer screening nationwide. The product, a Computer Assisted Diagnostic (CADx) software for lung cancer diagnosis, is the first diagnostic platform to gain regulatory clearance in its class



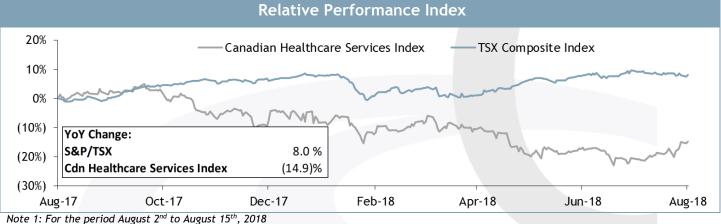
<u>Canadian Devices and Diagnostics Constituents</u>: CRH Medical Corporation, TSO3 Inc., Titan Medical Inc., Opsens Inc., Neovasc Inc., ChroMedX Corp., Profound Medical Corp., Covalon Technologies Ltd., Spectral Medical Inc., Hamilton Thorne Ltd.



CANADIAN HEALTHCARE SERVICES

News Scan¹

- Last twelve-month performance of the Canadian Healthcare Services Index decreased 14.9%, while the TSX Composite Index increased 8.0% over the same period. In August, the following occurred in the Canadian healthcare services space:
- On August 15th, <u>Akumin Inc.</u>, a provider of imaging and diagnostic procedures, announced that it acquired 11 freestanding, outpatient diagnostic imaging centers operated by <u>Rose Radiology Centers</u> in the Tampa Bay, Florida area. Akumin paid US\$25 million in cash, and the centers are expected to add approximately US\$27.5 million of revenue, and US\$4.8 million of EBITDA, based on the last twelve-month period ended March 31, 2018
 - On August 15th, <u>Akumin Inc.</u> announced that its subsidiary, <u>Akumin Corp.</u> closed credit facilities for US\$130 million. The proceeds of the term loan were used to repay existing credit facilities of approximately US\$74.6 million and to pay the purchase price of US\$25 million for its same-day announced acquisition of 11 diagnostic centers
- On August 13th, <u>Ascent Industries Corp.</u>, a licensed producer under the Access to Cannabis for Medical Purposes Regulations of <u>Health Canada</u>, announced the formation of its Health and Medical Services division under its wholly-owned subsidiary <u>AIC</u> <u>Health Services Corp.</u> AIC Health is developing a new model for providing multidisciplinary, patient-centric, full-service health care to patients in Canada with a mandate to develop a network of medical clinics that provide general and specialized health care services
- On August 7th, <u>AlayaCare</u>, a provider of home healthcare software solutions, announced a Series B investment of C\$13.8 million led by <u>Inovia Capital</u>. The financing will be used to fund AlayaCare's continued expansion with a focus on the US market and continued investment in its proprietary technology platform



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

Health Corporation



CANNABIS

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News Scan¹ The ACMPR has licensed 115 cannabis producers. Last twelve-month performance of the Cannabis index was about 134.5%, dwarfing the 8.0% gain of the TSX Composite Index over the same period. Highlights of cannabis news for August 2018: On August 15th, Canopy Growth and Constellation Brands announced a significant expansion of their strategic partnership, with Constellation increasing its ownership interest in Canopy to 38% by acquiring 104.5 million shares, totalling proceeds of about C\$5 billion. The shares will be acquired at C\$48.60 per share, representing a 51.2% premium to the previous day closing price. Constellation will also receive warrants that, if exercised, would provide at least an additional C\$4.5 billion On August 9th, Canopy Growth announced the acquisition of all remaining outstanding shares of its Chilean in-market entity, Spectrum Cannabis Chile SpA. This transaction supports its plans to expand within the Latin America region On August 7th, Canopy Growth announced that it completed the acquisition of Canopy Health Innovations (CHI) including its subsidiary, Canopy Animal Health (CAH). The company also received approval from Health Canada to research the effectiveness of cannabidiol (CBD) to treat anxiety in certain animals On August 14th, Aurora Cannabis announced it completed the acquisition of Anandia Laboratories, a cannabis-focused science company. Anandia is also currently developing a purpose-build Cannabis Innovation Centre in Vancouver. The acquisition is set to boost Aurora's scientific and research capabilities

- On August 8th, Aurora Cannabis announced that it entered into an exclusive license agreement with Alcanna, whereby Alcanna has exclusive rights to open retail cannabis stores under the brand name "Aurora" across Canada. The company expects to open 37 Aurora stores
- On August 7th, Aurora Cannabis announced that it intends to acquire the cannabis business of HotHouse Consulting, a provider of advanced greenhouse consulting services, to further specialize in hybrid greenhouse growing techniques
- On August 13th, Golden Leaf Holdings announced it signed a definitive agreement to acquire the assets of Tahoe Hydroponics Company for C\$52.4 million. The Tahoe acquisition will give Golden Leaf an immediate foothold in the state of California with a ~28,000 sq ft facility under development in Sacramento
- On August 9th, Auxly Cannabis (formerly Cannabis Wheaton) announced its subsidiary Dosecann successfully obtained a Dealer's License for Controlled Drugs and Substances from Health Canada. The license allows Dosecann to serve as a central mid-stream hub to Auxly and its subsidiaries in the development and manufacturing of value-added cannabis products
- On August 8th, Aphria announced that it signed a Manufacturer's Representative agreement with We Grow BC, a Vancouver-based licensed producer of premium cannabis, to become We Grow's exclusive sales representative across Canada
- On August 8th, CannTrust Holdings, announced that its accelerating its exclusive partnership with Apotex, the largest Canadian-owned generic pharmaceutical company. The partnership is developing alternate dosage formats for medical cannabis products, which aims to advance CannTrust's leadership in the medical cannabis market in Canada
- On August 8th, Invictus MD announced that it signed a commitment letter for a C\$25.5 million financing arrangement with ATB Financial to accelerate the construction of its cannabis cultivation facilities at Acreage Pharms in Alberta



Cannabis Index Constituents: Canopy Growth, Aurora Cannabis, Aphria, CannTrust Holding, Auxly Cannabis Group, OrganiGram Holdings, The Supreme Cannabis Company, The Hydropothecary

Note 1: For the period August 2nd to August 15th, 2018





Origin Merchant Partners

220 Bay Street, Suite 1500 P.O. Box 23 Toronto, Ontario M5J 2W4

OMP Healthcare Team:

Cathy Steiner

Principal T: 416-775-3602 Cathy.Steiner@originmerchant.com Jim Osler Principal T: 416-800-0784 jim.osler@originmerchant.com

Jim Meloche

Principal T: 416-800-0873 Jim.meloche@originmerchant.com

