



Prometic Life Sciences Inc.

Annual Information Form

Year ended December 31, 2016

March 23, 2017

**Table of Contents**  
**Annual Information Form**

Year ended December 31, 2016

1.	FORWARD-LOOKING STATEMENTS .....	3
2.	MARKET AND INDUSTRY DATA.....	4
3.	TRADEMARKS .....	4
4.	CORPORATE STRUCTURE .....	4
4.1.	Name and Incorporation.....	4
4.2.	Intercorporate Relationships .....	4
5.	GENERAL DEVELOPMENT OF THE BUSINESS .....	5
5.1.	Overview .....	5
5.2.	Three-Year History .....	6
6.	DESCRIPTION OF THE BUSINESS .....	13
6.1.	General.....	13
6.2.	Trends .....	21
6.3.	Objectives and R&D .....	23
6.4.	Commercial Applications, Products and Services .....	24
6.5.	Competitive Conditions.....	28
6.6.	Raw Materials, Components .....	28
6.7.	Intellectual Property Rights.....	28
6.8.	Product Development .....	29
6.9.	Research and Development .....	29
6.10.	Environmental Protection .....	29
6.11.	Employees .....	30
7.	RISKS AND UNCERTAINTIES RELATED TO PROMETIC’S BUSINESS.....	30
8.	DIVIDENDS .....	45
9.	DESCRIPTION OF CAPITAL STRUCTURE.....	45
9.1.	Common Shares .....	45
9.2.	Preferred Shares .....	46
10.	MARKET FOR SECURITIES .....	47
10.1.	Trading Price and Volume .....	47
11.	ESCROWED SECURITIES.....	47
12.	DIRECTORS AND EXECUTIVE OFFICERS .....	48
12.1.	Directors and Executive Officers .....	48
12.2.	Independence .....	54
12.3.	Security Holdings.....	55
12.4.	Cease Trade Orders, Bankruptcies, Penalties or Sanctions.....	55
12.5.	Conflicts of Interest.....	56
13.	LEGAL PROCEEDINGS AND REGULATORY ACTIONS .....	56
14.	INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS .....	56
15.	TRANSFER AGENT AND REGISTRAR.....	57
16.	MATERIAL CONTRACTS .....	57
17.	INTERESTS OF EXPERTS .....	57
18.	AUDIT & RISK COMMITTEE.....	58
19.	EXTERNAL AUDITOR SERVICES FEES.....	59
20.	ADDITIONAL INFORMATION .....	60

This Annual Information Form is dated March 23, 2017 and, unless it is stated otherwise, all the information disclosed herein is provided as of December 31, 2016, the end of Prometic's most recent financial year.

As used in this Annual Information Form, unless the context otherwise requires or indicates: (i) the "Corporation" or "Prometic" or "we" refer collectively to Prometic Life Sciences Inc. and its subsidiaries and predecessors; and (ii) all references to "\$" or dollars are in Canadian dollars unless otherwise specified.

## 1. FORWARD-LOOKING STATEMENTS

This Annual Information Form contains forward-looking statements about Prometic's objectives, strategies, financial condition, future performance, results of operations and businesses as of the date of this Annual Information Form.

These statements are "forward-looking" because they represent Prometic's expectations, intentions, plans and beliefs about the markets the Corporation operates in and on various estimates and assumptions based on information available to its management at the time these statements are made. Without limiting the generality of the foregoing, words such as "may", "will", "expect", "believe", "anticipate", "intend", "could", "would", "estimate", "continue", "plan" or "pursue", or the negative of these terms, other variations thereof or comparable terminology, are intended to identify forward-looking statements although not all forward-looking information contains these terms and phrases. Forward-looking information is provided for the purposes of assisting the reader in understanding the Corporation and its business, operations, prospects and risks at a point in time in the context of historical and possible future developments and therefore the reader is cautioned that such information may not be appropriate for other purposes.

Actual events or results may differ materially from those anticipated in these forward-looking statements if known or unknown risks affect our business, or if our estimates or assumptions turn out to be inaccurate. Such risks and assumptions include, but are not limited to, Prometic's ability to develop, manufacture, and successfully commercialize value-added pharmaceutical products, regulatory approvals, the availability of funds and resources to pursue research and development ("R&D") projects, the successful and timely completion of clinical studies, our ability to take advantage of business opportunities in the pharmaceutical industry, reliance on key personnel, collaborative partners and third parties, our patents and proprietary technology, our ability to access capital, the use of certain hazardous materials, the availability and sources of raw materials, currency fluctuations, the value of our intangible assets, negative operating cash flow, legal proceedings, uncertainties related to the regulatory process, general changes in economic conditions and other risks related to Prometic's industry. More detailed assessment of the risks that could cause actual events or results to materially differ from our current expectations can be found in this Annual Information Form under the heading "Risks and Uncertainties Related to Prometic's Business".

Although Prometic has attempted to identify important factors that could cause actual actions, events or results to differ materially from those described in forward-looking statements, there may be other factors that cause actions, events or results not to be as anticipated, estimated or intended. Therefore, there can be no assurance that forward-looking statements will prove to be accurate as actual results and future events could differ materially from those anticipated in such statements. Accordingly, you should not place undue reliance on forward-looking statements.

As a result, Prometic cannot guarantee that any forward-looking statement will materialize. Prometic assumes no obligation to update any forward-looking statement even if new information becomes available, as a result of future events or for any other reason, unless required by applicable securities laws and regulations.

## 2. MARKET AND INDUSTRY DATA

We have obtained the market and industry data presented herein from a combination of third-party sources and the estimates of management. Although we believe that these third-party sources and our management estimates are reliable, the accuracy and completeness of such data is not guaranteed and has not been verified by any independent sources. Market and industry data, including estimates and projections relating to size of market and market share, is inherently imprecise and cannot be verified due to limitations on the availability and reliability of data inputs, the voluntary nature of the data gathering process and other limitations inherent in any market research or other survey. Management's estimates are based on internal research, its knowledge of the relevant market and industry and third party sources. While we are not aware of any misstatements regarding the market and industry data presented herein, such data involve risks and uncertainties and are subject to change based on various factors, including those factors discussed under the headings "Forward-Looking Statements" and "Risks and Uncertainties Related to Prometic's Business".

## 3. TRADEMARKS

This Annual Information Form includes registered and unregistered trademarks such as Prometic™, Mimetic Ligand™, PPPS™, PrioClear™, Purabead® which are protected under applicable intellectual property laws and are the property of Prometic. Solely for convenience, our trademarks referred to herein and in other publicly filed documents may appear without the ® or ™ symbol, but such references are not intended to indicate, in any way, that we will not assert our rights to the fullest extent under applicable law. All other trademarks used herein are the property of their respective owners.

## 4. CORPORATE STRUCTURE

### 4.1. Name and Incorporation

Prometic was incorporated on October 14, 1994 under the Canada Business Corporations Act (the "CBCA") under the name Innovon Life Sciences Holdings Limited.

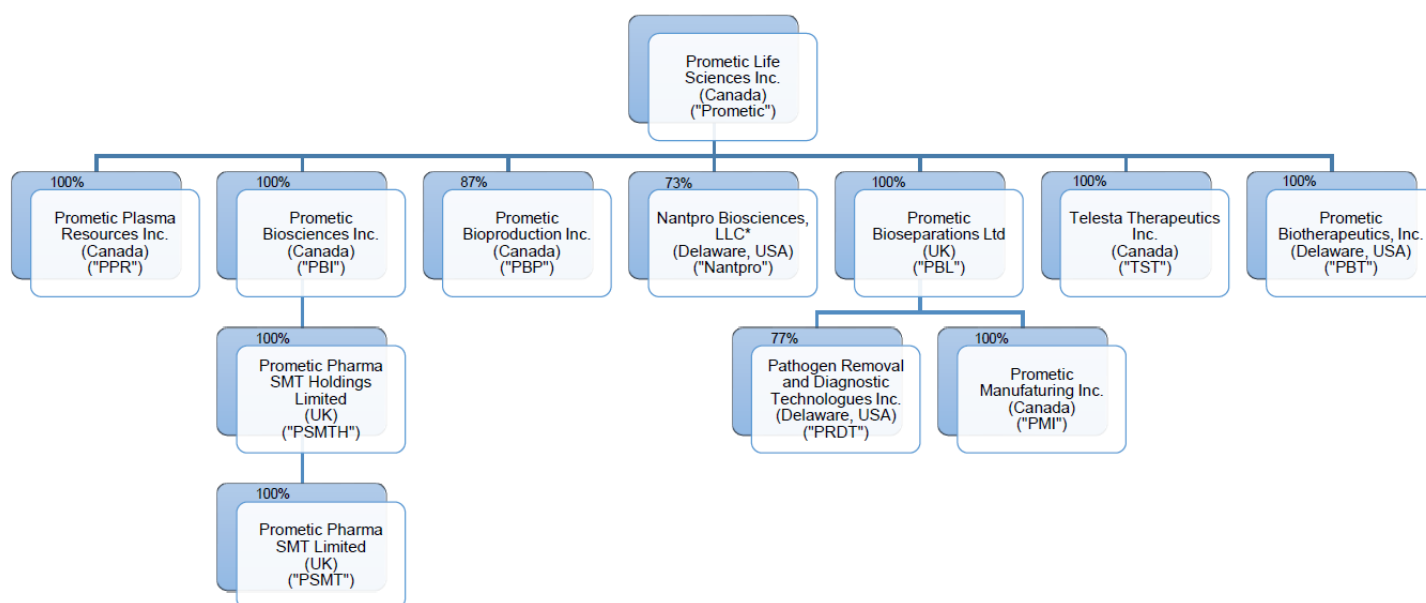
On December 21, 1995, the Corporation amended its articles of incorporation (the "Articles") to remove the private company restrictions. On June 6, 1996, the Corporation amended the provisions pertaining to the minimum and maximum number of directors. On April 10, 1995, October 10, 1995, June 19, 1997 and August 14, 1997, the Corporation made adjustments to its authorized share capital. On May 19, 1998, the Corporation changed its name to Prometic Life Sciences Inc. and simplified its authorized share capital structure such that the Corporation was authorized to issue an unlimited number of subordinate voting shares, 20,000,000 multiple voting shares and an unlimited number of preferred shares, issuable in series. On February 16, 2000, the Corporation created its initial two series of preferred shares. On May 15, 2008, the Corporation again amended its share capital by re-designating its subordinate voting shares into common shares, and repealing its multiple voting shares. On January 25, 2013, the Corporation removed the authorized preferred shares from its share capital.

The Corporation intends to pass a special resolution of the shareholders at the annual and special meeting of the shareholders of the Corporation to be held on May 10, 2017 to amend its Articles to provide that the directors of the Corporation may appoint one or more additional directors in accordance with the CBCA prior to the next annual meeting of the shareholders of the Corporation.

As at the date hereof, its head and registered office is located at 440 Armand-Frappier Blvd., Suite 300, Laval, Québec, H7V 4B4, Canada.

## 4.2. Intercorporate Relationships

The Corporation is structured as a parent company with seven material separate operating divisions (Prometic Biotherapeutics, Inc. ("**PBT**"), Prometic Biosciences Ltd. ("**PBL**"), Prometic Plasma Resources Inc. ("**PPR**"), Prometic Biosciences Inc. ("**PBI**"), Prometic Bioproduction Inc. ("**PBP**"), NantPro Biosciences, LLC ("**NantPro**") and Telesta Therapeutics Inc. ("**Telesta**"), which all are operated through subsidiaries directly controlled by the Corporation and one of which (Prometic Pharma SMT Limited ("**PSMT**") is operated through an entity indirectly held via a holding company (Prometic Pharma SMT Holdings Limited ("**PSMTH**") of a subsidiary of the Corporation (PBI). The following chart indicates the jurisdiction of incorporation of the Corporation's above-mentioned direct and indirect material operating divisions and principal subsidiaries, as well as the voting interest (expressed as a percentage) beneficially owned, controlled or directed by the Corporation in each subsidiary.



\* Subsidiary that has assets or revenues representing more than 10% of the consolidated assets or consolidated revenues of the Corporation.

## 5. GENERAL DEVELOPMENT OF THE BUSINESS

### 5.1. Overview

Prometic is an established biopharmaceutical company with widely recognized expertise in bioseparations, plasma-derived therapeutics and small-molecule therapeutics development. Prometic offers its bioseparation technologies and expertise for large-scale purification of biologics, drug development, proteomics and the elimination of pathogens to industry leaders and uses its own affinity technology that provides for highly efficient extraction and purification of therapeutic proteins from human plasma to develop and commercialize plasma-derived therapeutics. Prometic is also active in developing its own novel small-molecule therapeutic products targeting unmet medical needs in the fields of fibrosis, (targeting, inter alia, the lungs, liver, heart and kidney) as well as diabetes, anemia and autoimmune diseases.

Headquartered in Laval (Canada), Prometic has R&D facilities in the United Kingdom ("**UK**"), the United States ("**USA**") and Canada, manufacturing facilities in the UK and Canada and corporate and business

development activities in the UK, Canada, USA and Europe. Prometic's common shares (the "**Common Shares**") trade on the Toronto Stock Exchange ("**TSX**") under the symbol "PLI" and the OTCQX International under the symbol "PFSCF".

## 5.2. Three-Year History

### 2016

#### *Corporate*

**February.** The Corporation secured a follow-on investment from Structured Alpha LP ("**Structured Alpha**"), an affiliate of Peter J. Thomson's investment firm, Thomvest Asset Management Inc. ("**Thomvest**"), consisting of a \$30 million original issue discount loan (the "**New OID Loan**").

The New OID Loan is in addition to each of the two existing original issue discount loans with Structured Alpha in the amounts of \$10 million and \$20 million (the "**Existing OID Loans**"). The New OID Loan is secured by all of Prometic's (and some of its subsidiaries') assets, excluding its patent portfolio. The face value of the New OID Loan implies a compounded annual interest rate of 8%. No interest or principal is required to be repaid prior to July 31, 2022. As partial consideration for the New OID Loan, Prometic granted Structured Alpha 11,793,380 warrants to purchase Common Shares at an exercise price of \$4.70 per Common Share with a term expiring on July 31, 2022. The proceeds received by Prometic from the aggregate exercise of all such warrants would be sufficient to repay the New OID Loan in its entirety. No material additional security or covenants have been granted to Structured Alpha over those already in place in connection with the Existing OID Loans.

Also, in February, Prometic closed its bought deal public offering of Common Shares (the "**Offering**") through a syndicate of underwriters led by RBC Capital Markets and Canaccord Genuity Corp., and which included Scotiabank, CIBC Capital Markets, National Bank Financial Inc., Paradigm Capital Inc. and Beacon Securities Limited (collectively, the "**Underwriters**"). Prometic issued 19,400,000 Common Shares in connection with the Offering at a price of \$3.10 per share for aggregate gross proceeds of \$60,140,000. In consideration for the services rendered by the Underwriters under the Offering, the Underwriters received a cash commission representing 5% of the gross proceeds of the Offering.

**October.** Prometic announced that it had closed the acquisition of all the issued and outstanding common shares of Telesta by way of a plan of arrangement under the CBCA (the "**Acquisition**") for a consideration of \$0.14 per Telesta common share payable in Common Shares. The number of Common Shares issued by Prometic was based on the volume-weighted average closing price ("**VWAP**") of Prometic's common shares for the five trading days prior to the closing date of the Acquisition. At the end of trading on the TSX on Friday, October 28, 2016, the 5 day VWAP of Prometic's common shares was \$2.98. Accordingly, each Telesta common share was acquired for 0.04698 Common Share.

#### *Plasma-Derived Therapeutics*

**June.** Prometic reported that the US Food and Drug Administration ("**FDA**") had granted a Fast Track designation to Prometic for its plasminogen drug candidate, then in a phase 2/3 clinical trial in patients suffering from congenital Plasminogen deficiency.

**August.** Prometic announced that it had completed the enrolment of the adult patient population (50 adult patients) in its pivotal IVIG phase 3 clinical trial for the treatment of primary immunodeficiency diseases ("**PIDD**"). The ongoing pivotal phase 3 clinical trial is an open label, single arm, two-cohort multicenter study investigating the safety, tolerability, efficacy and pharmacokinetics of Prometic's plasma derived IVIG in a total of 75 patients suffering from PIDD, including 50 adults (cohort 1) and 25 children (cohort 2).

Prometic announced that it had completed enrolment of the congenital plasminogen deficient patients in its pivotal phase 2/3 clinical trial required for the accelerated regulatory approval pathway with the FDA.

**September.** Prometic announced that it would be pursuing tympanic membrane perforations (“**TMP**”), as one of its new plasma-derived plasminogen related targeted clinical indications.

**October.** Prometic announced that its pivotal phase 2/3 clinical trial in patients with plasminogen deficiency had met its primary and secondary endpoints with the intravenous plasminogen treatment. In addition to being safe, well tolerated and without any drug related serious adverse events, Prometic’s plasminogen treatment achieved a 100% success rate of its primary end point, namely, a targeted increase in the blood plasma concentration level of plasminogen as a surrogate target. Moreover, all patients who had active visible lesions when enrolled in the trial had complete healing of their lesions within weeks of treatment, a 100% response rate for this secondary end point.

**November.** During an Analysts Day in New York, Prometic disclosed its intent to focus on expanding the clinical uses of plasminogen as a priority over the coming years. In addition to the treatment of wounds such as diabetic foot ulcers and tympanic repair, acquired plasminogen deficiency in critical care such as severe burns was provided as an example. The expansion of plasminogen development program enables the Corporation to target multiple clinical indications with unmet medical needs with the same proprietary API via different formulations and presentations. Combined with market exclusivity and significant growth opportunity, plasminogen is prioritized over advancing certain previously disclosed follow-ons therapeutics with competitive landscapes such as C1-INH.

**December.** Prometic announced that it had initiated the rolling submission of its Biologics License Application (“**BLA**”) for plasminogen with the FDA for treatment of patients with plasminogen congenital deficiency.

#### *Small Molecule Therapeutics*

**March.** Prometic announced that the preliminary analysis of new pro-inflammatory biomarkers in blood and urine samples from the patients in the on-going, open label, phase 2, metabolic syndrome and Type 2 diabetes clinical trial provided additional evidence of PBI-4050’s pharmacological and clinical activity in humans. In December 2015, the Corporation reported the statistically and clinically significant decrease in HbA1C observed in the first 11 patients enrolled who had completed the 12 week study. Overall the patients experienced improved blood glucose control as measured by HbA1C (average decrease of -0.6% p=0.03), with 10 of the 11 experiencing a decrease in HbA1c incremental to that achieved by standard-of-care drug regimes.

**April.** Prometic presented new data at the 2016 European Association for the Study of the Liver (EASL)’s 51st Annual Meeting – The International Liver Congress (ILC) in Spain. The new data confirmed that PBI-4050’s anti-fibrotic effect demonstrated in the livers of different animal models has been successfully reproduced in human hepatic stellate cells (“**HHSC**”) during in vitro preclinical experiments designed to simulate fibrogenesis in the liver. PBI-4050 was found to down-regulate key pro-fibrotic biomarkers considered to be driving the fibrotic process in nonalcoholic steatohepatitis (“**NASH**”).

**May.** Prometic reported that it had been authorized to commence the clinical trial of its orally active anti-fibrotic lead drug candidate, PBI-4050, in patients suffering from cystic fibrosis (“**CF**”), following the clinical trial application clearance by Health Canada. The objectives of this 24 week randomized, double-blind, and placebo-controlled phase 2 study include the evaluation of the effects of PBI-4050 on the pancreatic and lung functions in 90 CF patients.

**October.** Prometic announced that the Drug Safety Monitoring Board (“**DSMB**”) recommended that patient enrolment should continue in the Corporation’s ongoing Alström syndrome phase 2 clinical trial. This recommendation followed the DSMB’s review of the safety data accumulated in the first eight Alström syndrome patients that had received treatment with PBI-4050. The DSMB determined that no safety or tolerability issues had been observed in these patients. The first five patients (100%) who completed 12 weeks of treatment with PBI-4050 had a reduction of liver fibrosis, as measured by transient elastography (FibroScan®).

Prometic announced that its phase 2 clinical trial in patients with metabolic syndrome and type 2 diabetes had been completed and had met its primary and secondary endpoints. In addition to safety and tolerability, the study was designed to evaluate the effect of PBI-4050 on metabolic syndrome parameters as well as on pro-inflammatory/fibrotic and diabetic biomarkers in blood and urine. In this open label phase 2 clinical trial, PBI-4050 (800 mg) was administered once daily to 24 patients for a period of 12 weeks. For instance, the 15 patients with a screening HbA1c  $\geq 7.5$  experienced a mean decrease of  $-0.75\%$  ( $p = 0.0004$ ) while the 9 patients with a screening HbA1c  $\geq 8.0\%$  experienced a mean decrease of  $-0.9\%$  ( $p = 0.007$ ). The 10 patients who participated in the study's 12 week extension had a mean HbA1c of 7.7 at screening and experienced a reduction of  $-0.8\%$  at week 12: this reduction was maintained at week 24. PBI-4050 had been well tolerated with no serious drug related adverse events.

**November.** Prometic reported that it had received clearance by Health Canada to commence a placebo-controlled phase 2 clinical trial with its PBI-4050, the company's orally active, lead small molecule anti-fibrosis drug candidate, in patients with metabolic syndrome and type 2 diabetes.

Prometic announced positive interim results from its Open Label phase 2 clinical trial in patients suffering from idiopathic pulmonary fibrosis ("**IPF**"). In addition to demonstrating that PBI-4050 is safe and well tolerated in patients suffering from IPF, the objective of this study was to provide early evidence of clinical benefits of PBI-4050 treatment whether used alone or in addition to either nintedanib or pirfenidone. Forty patients were enrolled in the study in 6 sites across Canada. At that time, the Corporation was reporting on the first 30 patients that had completed their 12 weeks of treatment. In February 2017, Prometic announced positive results from its completed open label phase 2 clinical trial in subjects suffering from IPF. In addition to demonstrating that PBI-4050 is safe and very well tolerated, an objective of this study was to seek early evidence of a clinical benefit with PBI-4050 treatment, whether administered alone or in addition to either of the drugs approved for the treatment of IPF, nintedanib or pirfenidone. These results confirm the preliminary results previously announced by Prometic on November 17, 2016, following the first 30 subjects' completion of 12 weeks of treatment.

Prometic presented new data at the American Society of Nephrology's ("**ASN**") Annual Meeting currently underway in Chicago, with respect to Prometic's anti-fibrotic and orally active lead drug candidate, PBI-4050.

## **2015**

### *Corporate*

**March.** On March 31, 2015, the Corporation, certain of its subsidiaries and Structured Alpha entered into (i) an amended and restated loan agreement, which amended and restated the loan agreement originally dated as of July 31, 2014 between the same parties, and (ii) a second amended and restated loan agreement, which amended and restated the amended and restated loan agreement dated as of July 31, 2014, which in turn amended and restated the loan agreement originally dated as of September 10, 2013 between the same parties (the foregoing March 31, 2015 agreements are herein collectively referred to as the "2015 Amended and Restated Loan Agreements"). The 2015 Amended and Restated Loan Agreements provided for several amendments in favour of the Corporation which, amongst others, included the extension of the maturity date of the loans made thereunder to July 31, 2022, a right of repayment of such loans commencing on September 13, 2018, and more flexibility in its affirmative and negative covenants. In consideration for the above modifications, the Corporation granted Structured Alpha 7,000,000 warrants to purchase the Common Shares at an exercise price of \$3.00 per Common Share. The warrants have an expiry date of July 31, 2022. The Corporation also granted Structured Alpha a pre-emptive right to participate in any future public offering or private placement of the Common Shares or securities convertible or exchangeable into Common Shares.

Prometic was added to the S&P/TSX Composite Index.



**May.** The Corporation closed a bought deal public offering of 19,250,000 Common Shares at \$2.60 per Common Share for gross proceeds of \$50,050,000 through a syndicate of underwriters led by Canaccord Genuity Corp., and which included RBC Dominion Securities Inc., Beacon Securities Limited, TD Securities Inc. and Paradigm Capital Inc.

The Corporation also completed the closing of the over-allotment option to acquire an additional 2,887,500 Common Shares at a price of \$2.60 per over-allotment share, for gross proceeds of \$7,507,500.

**December.** The Corporation completed an internal corporate reorganization of its subsidiaries owning and exploiting the Small Molecule Therapeutics segment, which involved the centralization of key development and commercialization activities as well as the Small Molecule Intellectual Property (“**SMIP**”) in a newly created UK subsidiary of the Corporation, Prometic Pharma SMT Limited (“**PSMT**”). An intellectual property transfer agreement was entered into between PBI and PSMT whereby all of the SMIP (other than the Canadian SMIP) were transferred to PSMT.

The Corporation expects this reorganization to enable the Small Molecule Therapeutics business segment to execute its global drug development and commercialization strategy more effectively. The new structure intends to take advantage of the Corporation’s existing operations in the UK, which include R&D and executive management, while leveraging the business, financial, tax and accounting efficiencies therein.

#### *Bioseparation Technologies*

**February.** The Corporation announced that it had received an \$11.4 million purchase order for the supply of an affinity resin to an existing client, a global leader in the biotherapeutics industry. This was the second purchase order resulting from the license and long-term supply agreement previously announced on July 8, 2013. The affinity resin was manufactured by Prometic at its Isle of Man facility and supplied to the client throughout the second half of 2015 and the first half of 2016. Prometic’s client uses the resin for large-scale purification of a therapeutic protein product manufactured in large quantities. The last deliveries against this order were made during the second quarter of 2016.

**December.** The Corporation renewed its supply agreement with GlaxoSmithKline LLC. The renewed agreement followed the original supply agreement entered into between the parties in 2009.

#### *Plasma-Derived Therapeutics (Biologicals)*

**May.** The Corporation had selected C1-INH as its next plasma-derived drug candidate to be developed. The C1-INH protein is most commonly used for the treatment of hereditary angioedema, a rare genetic disorder in which C1-INH is lacking.

Prometic entered into a strategic manufacturing agreement with Emergent BioSolutions (“**Emergent**”). The long-term manufacturing agreement provided Prometic with access to additional cGMP capacity in an FDA-licensed facility, located in Winnipeg, Canada. Prometic would use this capacity for the development and manufacture of plasma-derived biopharmaceuticals using Prometic’s proprietary plasma purification platform, Plasma Protein Purification System (PPPSTM). The additional manufacturing capacity could provide the ability to process up to 250,000 liters of plasma annually with the potential for further expansion should the parties agree. This 15-year manufacturing agreement involves an initial annual minimum payment of approximately \$4M per year, rising to \$7M per year in 2018 and to \$9M per year by 2021, for an aggregate total of minimum fees exceeding \$100M over the life of the contract. This minimum payment secures a defined capacity. The agreement allows for a flexible approach for the use of resources up to that value, and any additional resources used beyond that minimum cost is to be charged on an as-used basis.

**August.** The Corporation was granted an orphan drug designation status for its human plasma-derived plasminogen drug for the treatment of plasminogen deficiency by the European Commission.

The Corporation successfully completed the first round of dosing of plasminogen deficient patients. Prometic's IV plasminogen was found to be safe, very well tolerated and there were no drug-related adverse events.

The Corporation closed the acquisition of Emergent's plasma collection center located in Winnipeg, Canada. The plasma collection center has started to operate under Prometic's ownership following the grant and receipt of the regulatory licenses by and from the requisite regulatory authorities. Prometic's plasma collection center is an FDA, EMEA and Health Canada licensed plasma collection facility conveniently located in close proximity to the existing Emergent Winnipeg based cGMP manufacturing facility.

**October.** The FDA completed its review and cleared the Investigational New Drug ("IND") application for Prometic's Intravenous Immunoglobulin ("IVIG") biological drug product for the treatment of primary immunodeficiency diseases ("PID").

**November.** The Corporation announced that its plasma-derived plasminogen replacement therapy, currently in phase 1 clinical trial in the USA, had been successfully used to treat a plasminogen-deficient infant in critical condition in an intensive care unit at the Altona Children's Hospital located in Hamburg, Germany. The plasminogen was administered by a team from the Department of Pediatric Haematology and Oncology at the University Medical Center, Hamburg-Eppendorf, under the direction of Professor Reinhard Schneppenheim. The plasminogen and the protocol for its use recommended by Prometic enabled the team to quickly reach an efficacious concentration of plasminogen in the blood. Within a few days, a reduction of the lesions was observed, and after six weeks of therapy the lesions had markedly improved.

The Corporation entered into a strategic agreement with a Swedish company, Omnio AB ("Omnio"). The agreement provided Prometic with an exclusive proprietary intellectual property license as well as a comprehensive proprietary understanding of the use of plasminogen in the field of hard-to-treat wounds, such as diabetic foot ulcers.

The Corporation entered into a strategic partnership with ProThera Biologics Inc. for the development and commercialization of human plasma-derived Inter-alpha Inhibitor Proteins ("IAIP"). The agreements provided Prometic with global, exclusive intellectual property rights to commercialize products for two clinical indications and both companies have strategic interest in the other's IAIP-related therapeutic areas through a royalty-bearing cross-license agreement.

**December.** The Corporation presented safety, pharmacokinetic and clinical data from its plasma-derived plasminogen replacement therapy phase 1 clinical trial for the treatment of Congenital Plasminogen Deficiency at the American Society of Hematology annual conference in Orlando, Florida (ASH 2015). The results from the two cohorts of patients enrolled in the phase 1 trial confirmed that Prometic's plasminogen replacement therapy was safe, well tolerated and without any related serious adverse events. Moreover, there were no plasminogen antibodies detected and the results confirmed the established therapeutic dose of 6 mg/kg.

#### *Small Molecule Therapeutics*

**January.** The Corporation received CTA clearance from Health Canada. Its orally active lead drug candidate, PBI-4050, was approved for the Corporation to commence the clinical trial in patients suffering from metabolic syndrome and resulting Type 2 diabetes.

**February.** The Corporation's orally active anti-fibrotic lead drug candidate, PBI-4050, was approved by Health Canada and the Corporation could commence the clinical trial in patients suffering from idiopathic pulmonary fibrosis ("IPF"), following the CTA clearance by Health Canada.

The Corporation received an orphan drug designation status for its orally active anti-fibrotic lead drug candidate, PBI-4050, for the treatment of IPF from the FDA.

**March.** The Corporation successfully completed its PBI-4050 phase 1b multi-dose clinical trial in patients with chronic kidney disease. Prometic's orally active lead drug candidate, PBI-4050, was found to be safe and well tolerated without any serious adverse events reported.

**May.** The Corporation presented new pre-clinical data at the American Thoracic Society 2015 International Conference held in Denver, USA, on PBI-4050, its orally active anti-fibrotic drug candidate in phase 2 clinical trials for the treatment of IPF. In the gold standard animal model used to emulate pulmonary fibrosis in humans, PBI-4050 performed favorably compared to Nintedanib, one of the two FDA-approved products for such medical use. PBI-4050 significantly reduced the amount of tissue scarring observed in the lungs of non-treated animals. In this model, the combination of PBI-4050 and Nintedanib did not provide a synergistic superior outcome, in contrast to the previously reported synergistic and positive effect on reduction of fibrotic markers seen with the combination of PBI-4050 and Pirfenidone.

**June.** The Corporation presented new data at the European Renal Association (ERA) annual meeting in London, UK. The new data confirmed that PBI-4050's anti-fibrotic effect demonstrated in the kidney in several different animal models has been successfully reproduced in human kidney cell lines during in vitro experiments. The data presented at the ERA annual meeting summarized the effect of PBI-4050 on Normal Human Dermal Fibroblasts ("NHDF") and Human Epithelial Proximal Tubule Cells (HK-2) ("human kidney cells") in in vitro experiments designed to simulate fibrosis. PBI-4050 was found to regulate the pro-fibrotic growth factors and the remodeling enzymes in both the NHDF and human kidney cells in the same manner as observed in animals.

**August.** The Corporation reported that its PBI-4050 had been confirmed to be safe and well tolerated in the first 12 metabolic syndrome with associated type 2 diabetes patients, following review of the safety data by the Data Safety Monitoring Board. Prometic proceeded with the enrollment of an additional 24 patients, as planned in the study protocol design.

**October.** An orphan drug designation status had been granted to the Corporation for its lead drug candidate, PBI-4050, for the treatment of IPF, by the European Commission.

The Corporation's clinical trial application ("CTA") for its anti-fibrotic lead drug candidate PBI-4050 in patients suffering from a condition associated with type 2 diabetes and severe multi-organ fibrosis (Alström Syndrome) was cleared by the Medicines and Healthcare Products Regulatory Agency ("MHRA") in the UK. This is an open-label, single-arm, phase 2 study initially recruiting 20 patients. Each patient will be evaluated against their respective baseline which is very well documented given the severity of their medical condition. The initial treatment period is 6 months with a possibility to extend the study. The objectives of the study are to evaluate the safety and tolerability of PBI-4050, and the effects of PBI-4050 on key organ function, disease progression and inflammatory/fibrotic markers.

**December.** The Corporation decided to close patient enrollment in its phase 2 open label study in patients suffering from type 2 diabetes and metabolic syndrome and to transition to a pivotal placebo-controlled phase 2 study in patients suffering from type 2 diabetes. The Corporation reported the statistically and clinically significant decrease in HbA1C observed in the first 11 patients enrolled who had completed the 12 week study. Overall the patients experienced improved blood glucose control as measured by HbA1C (average decrease of -0.6% p=0.03), with 10 of the 11 experiencing a decrease in HbA1c. In patients with HbA1c values greater than 7.5% at screening, this decrease in HbA1c exceeded 1%, a performance that compares very favorably to drugs already approved for the treatment of diabetes.

The Corporation announced its plans to initiate a double-blind placebo controlled phase 2 clinical trial in patients suffering from cystic fibrosis (CF) and related diabetes and liver steatosis. CF is a condition which affects approximately 70,000 individuals in North America and compromises their pulmonary, pancreatic and hepatic functions.

## **2014**

### *Corporate*

**February.** The Corporation appointed Dr. John Moran as its new Chief Medical Officer. The Corporation also entered into a new agreement with a leading vaccines company for the development of an affinity adsorbent and associated purification process for the production of a novel vaccine product.

**March.** The Corporation received approximately \$3.2 million via the repayment of the amended and restated loan entered into in March 2010 by Prometic and InvHealth Holding Inc., a corporation wholly-owned and controlled by Mr. Pierre Laurin, President and Chief Executing Officer of Prometic.

**May.** The Corporation increased its ownership in NantPro following the amendment of its related corporate and commercial agreements with NantPharma, LLC ("**NantPharma**"). The amended agreements provide Prometic with a greater portion of the future value and revenues associated with the development and sales of IVIG in the USA.

**July.** The Corporation secured a follow-on investment from Thomvest, a Toronto-based investment vehicle of Peter J. Thomson, consisting of a \$20 million loan. As partial consideration for the loan, Prometic granted Thomvest 16,723,807 warrants with an exercise price of \$1.87 per Common Share. Prometic used part of the proceeds from this investment for the development and manufacture of both additional and existing plasma-derived orphan drugs, the advancement of the ongoing PBI-4050 clinical programs, as well as the repayment of secured debt provided by certain shareholders. The rights and obligations of Thomvest as lender under such loan, as well as its rights and obligations as holder of such warrant, were assigned by Thomvest to Structured Alpha effective October 1, 2014.

**August.** The Corporation announced the promotion of Mr. Bruce Pritchard to the newly created position of Chief Operating Officer.

**December.** The Corporation closed a public offering of 13,200,000 Common Shares at a price of \$1.90 per Common Share for aggregate gross proceeds of \$25,080,000. The Corporation also closed the over-allotment option whereby it issued an additional 1,980,000 Common Shares at a price of \$1.90 per Common Share, for gross proceeds of \$3,762,000.

### *Bioseparation Technologies*

**June.** The Corporation received a \$5.6 million purchase order under its ongoing supply agreement with Octapharma, a leading, Swiss independent global plasma fractionation company that specializes in human proteins, relating to the purchase of PrioClear™, a proprietary prion capture resin incorporated into Octapharma's manufacturing process for its solvent/detergent treated plasma product, OctaplasLG®. OctaplasLG® is currently approved for marketing in USA and several European countries.

**July.** PBL entered into an agreement with one of its existing multinational clients, a global leader in the biotherapeutics industry, relating to the development and scale-up of a new affinity resin and associated manufacturing process in order to enhance the quality and purity of an existing biopharmaceutical product manufactured in large quantities.

### *Plasma-Derived Therapeutics (Biologicals)*

**January.** The Corporation announced the achievement of the second manufacturing milestone related to its strategic agreement with Hematech Biotherapeutics Inc. ("**Hematech**"), triggering a \$1 million payment

to Prometic. This milestone was achieved following the successful completion of the first large-scale production run at its PBP plasma purification facility located in Laval, Quebec.

**July.** The Corporation announced that it would launch fibrinogen for commercial sales during the fourth quarter of 2014 after its successful scale-up at PBP's Laval facility. This announcement followed the previously-disclosed proteins already scheduled for production at PBP, namely plasminogen, IVIG and Alpha-1 Antitrypsin.

**October.** The FDA completed its review and cleared the IND application for Prometic's IV Plasminogen for the treatment of hypoplasminogenemia, or type I plasminogen deficiency. If approved, this product is intended to provide replacement therapy for patients who suffer from a congenital lack of the normal plasminogen protein and/or its functional activity, and are subject to life-long medical problems which currently have limited effective treatments.

**December.** The Corporation entered into definitive agreements with Generium Company Pharmaceuticals ("Generium") for several plasma-derived biopharmaceuticals to be manufactured and commercialized in Russia and the Commonwealth of Independent States (CIS). The strategic alliance includes the granting of manufacturing rights to Generium for several plasma-derived biopharmaceuticals using Prometic's proprietary Plasma Protein Purification System (PPPSTM) ("**PPPS**") technology. In addition, Prometic agreed to provide training and technical support to manufacture such biopharmaceuticals in a facility to be built and operated by Generium, in Russia. The design of the Generium plasma purification facility will be based on Prometic's Laval facility and is intended to have a plasma processing capacity of up to 600,000 litres per year. Construction of this facility has already commenced and is expected to be completed by the second half of 2018. Generium is responsible for funding the construction and operating costs of its new current GMP PPPSTM facility.

#### *Small Molecule Therapeutics*

**June.** The Corporation successfully completed its PBI-4050 phase 1 clinical trial in 40 healthy volunteers. Prometic's PBI-4050 was found to be safe and very well tolerated without any serious adverse events reported in any of the five cohorts tested. The objectives of this oral, double blind, placebo controlled, single ascending dose study were to demonstrate the safety and tolerability of PBI-4050 and to establish the pharmacokinetic profile of the drug candidate at different doses. The study design also included a component evaluating food effect on drug absorption. The trial was conducted in five cohorts of eight subjects. In each cohort, six subjects received PBI-4050 and two subjects received matching placebo.

**October.** Prometic announced that it would be pursuing IPF as one of its PBI-4050 orphan indications. This decision followed the completion of a favorable external review of the considerable anti-fibrotic preclinical data generated to date by an independent panel of world experts on idiopathic pulmonary fibrosis and the analysis of the current market landscape.

**November.** The Corporation reported that its small molecule lead compound PBI-4050 has been approved to commence clinical trials in patients suffering from Diabetic Kidney Disease ("**DKD**") following the CTA clearance by Health Canada. The initial phase of the clinical program was scheduled to commence in November, with eight DKD patients to be enrolled. The objectives of this double blind, placebo controlled, multi-dose study are to demonstrate the safety and tolerability of PBI-4050 and to compare the pharmacokinetic profile of the drug in DKD patients with severely impaired kidney function to that demonstrated in healthy volunteers.

## **6. DESCRIPTION OF THE BUSINESS**

### **6.1. General**

Prometic's operation is divided in two distinct business segments: the protein technologies segment comprising the Bioseparation Technologies and Plasma-Derived Protein Therapeutics businesses (the

“**Protein Technologies Segment**”) and the small-molecule therapeutics (the “**Small-Molecule Therapeutics Segment**”).

### ***Protein Technologies Segment***

Prometic has been historically known for its expertise in bioseparation, specifically for large-scale purification of biologics and the elimination of pathogens, to industry leaders. However, Prometic has also leveraged its own industry leading affinity chromatography technology to develop a highly efficient extraction and purification process of therapeutic proteins from human plasma in order to develop plasma-derived protein therapeutics and orphan drugs targeting unmet medical conditions and rare diseases. A multitude of rare diseases and medical conditions are known to be directly related to either missing, insufficient quantities of or non-functional proteins. Prometic’s proprietary PPPS™ manufacturing process technology allows for superior extraction and recovery capabilities of such valuable proteins from plasma. See “Plasma-Derived Therapeutics Segment”.

With all the necessary elements to accelerate the development of a strong product pipeline, Prometic continues to fully transition into a vertically integrated specialty biopharmaceutical corporation. At the core of this strategy resides the bioseparation technologies and products of the Corporation. The Corporation’s bioseparation products derive from its various affinity ligand platforms (Mimetic Ligands™ and peptide ligands) and its support matrices (Purabead®) to provide chromatography adsorbents for use in the capture and purification of protein therapeutics. A number of these bioseparation products are targeted at specific proteins such as the affinity resins that form the backbone of the PPPS™ process (specific affinity adsorbents for the capture of proteins such as clotting factors, plasminogen, fibrinogen, IVIG, alpha-1-antitrypsin and albumin); resins for the purification of recombinant albumin and albumin-fusion proteins (Mimetic Blue® SA and Albupure®), resins for the purification of polyclonal antibodies and related antibody fragments (Mabsorbent®, Fabsorbent™) and Insulin Adsorbent for the purification of Insulin and Insulin analogues. Other products target the capture and purification of certain groups of proteins such as glycoproteins (Aminophenyl boronate resins) and proteases (p-Aminobenzamidine resins). The Corporation also has products which target the capture and removal of certain types of contaminants such as endotoxin (Etoxiclear™), prions (Prioclear™) and isoagglutinins (Isoclear™), in addition to more generic products for general purification and polishing applications such as Ion-exchange resins, Hydrophobic Interaction adsorbents, Mimetic Ligand™ adsorbents and chromatography column hardware & screening kits. The Corporation also supplies a variety of custom products to clients who have sponsored the Corporation to develop and manufacture chromatography adsorbents for client-specific applications.

### ***Bioseparation Technologies***

Our subsidiaries PBL, Prometic Manufacturing Inc. (“**PMI**”) and Pathogen Removal and Diagnostic Technologies Inc. (“**PRDT**”) form the bioseparation technology portion of our business.

Prometic’s bioseparation technologies enable the targeted capture proteins directly from biological source materials to provide a highly efficient and cost-effective manufacturing processed for biopharmaceutical products.

The Corporation’s proprietary purification adsorbents and manufacturing processes for biological products are used by more than 30 companies in the pharmaceutical, biotechnology and medical industries, where Prometic’s clients employ this technology to purify proteins, remove impurities and pathogens, reduce manufacturing costs, and increase the yield of therapeutic products.

PBL develops and manufactures Prometic’s core bioseparations technologies and products. Its proprietary affinity adsorbents and Mimetic Ligand™ purification platform are used by numerous pharmaceutical and medical companies worldwide. As a result, manufacturing clients using Prometic’s bioseparation technologies benefit from reductions in their cost of goods and increases in product quality and safety. PBL’s technology has also been incorporated into various medical device products which

specifically capture and remove target molecules from biological fluids. PBL has recently expanded its manufacturing capacity for chromatography absorbents and now has the capability to produce >35,000 litres of product per annum to pharmaceutical GMP standard.

PRDT developed the prion capture technology platform that originated from Prometic's collaboration with the American Red Cross. PRDT's technology forms the basis of the P-Capt® filter, a prion reduction device developed with Prometic's commercial partner, MacoPharma, to increase the safety of red cell concentrate.

PRDT's platform technology has demonstrated its potential for additional uses in the purification of blood-derived products. For instance, PRDT technology has been incorporated by Octapharma into its manufacturing process for OctaplasLG® to further improve the prion safety margin for this plasma product. OctaplasLG® has obtained regulatory approvals in several European countries (including Germany and the UK), the USA and Australia.

PMI manufactures the agarose beads (Purabead®) that serve as a platform for many of PBL's affinity resins.

### *Plasma-Derived Protein Therapeutics*

Our subsidiaries PBT, PBP, NantPro and PPR operate the plasma-derived protein therapeutics (biologicals) portion of our business. Certain assets and human resources of our newly acquired subsidiary, Telesta Therapeutics Inc., may also be operated in the plasma-derived protein therapeutics portion of our business. Prometic is currently evaluating its options in relation to the former.

PBT develops manufacturing processes, based on PBL's affinity technology, to provide efficient extraction and purification of therapeutic proteins from human plasma. Prometic's PPPS™ multi-product sequential purification process, originally developed in collaboration with the American Red Cross, employs powerful affinity separation materials in a multi-step process to extract and purify commercially important plasma proteins in high yields and purity. This technology is key for extracting valuable proteins, which Prometic plans to commercialize with an emphasis on therapeutic products targeting orphan designated indications.

Prometic's IV Plasminogen is the first PPPS generated plasma-derived therapeutic to enter clinical trial stages.

In October 2014, the FDA had completed its review and cleared the IND application for Prometic's IV Plasminogen for the treatment of plasminogen congenital deficiency. If approved, this product is intended to provide replacement therapy for patients who suffer from a congenital lack of the normal plasminogen protein and/or its functional activity, and are subject to life-long medical problems which currently have limited effective treatments. The FDA also accepted that Prometic's proposed phase 2/3 clinical program for the IV Plasminogen provides an adequate surrogate endpoint for licensure using the accelerated approval pathway. To secure an accelerated pathway approval, a drug must treat a serious condition, provide a meaningful advantage over available therapies and demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit.

In addition to being granted orphan drug designation by the European Commission and FDA, Prometic has filed numerous patents to protect this biopharmaceutical asset. In completing its phase 2/3 trial in 2016, Prometic demonstrated that patients with plasminogen deficiency had met the study's primary and secondary endpoints when treated with the intravenous plasminogen treatment. In addition to being safe, well tolerated and without any drug related serious adverse events, Prometic's plasminogen treatment achieved a 100% success rate of its primary end point, namely, a targeted increase in the blood plasma concentration level of plasminogen as a surrogate target. Moreover, all patients who had active visible lesions when enrolled in the trial had complete healing of their lesions within weeks of treatment, a 100% response rate for this secondary end point.

Prometic initiated the rolling submission of its Biologics License Application (“**BLA**”) for plasminogen with the FDA for treatment of patients with plasminogen congenital deficiency in late 2016.

Prometic expects to file its completed BLA for plasminogen in a timely manner to receive FDA marketing approval in 2017.

Prometic’s IVIG is the second PPPS generated plasma-derived therapeutic to enter clinical trial stages.

NantPro is the entity responsible to develop and commercialize IVIG for treatment of primary immunodeficiency diseases (“**PIDD**”) in the USA. NantPro’s sister company, PBT, has been providing development services for NantPro consisting of pre-clinical activities, such as filing of the IND for IVIG for treatment of PIDD as well as preparing for and overseeing the on-going phase 3 clinical trial.

Prometic completed the enrolment of the adult patient population (50 adult patients) in its pivotal IVIG phase 3 clinical trial for the treatment of PIDD. The ongoing pivotal Phase 3 clinical trial is an open label, single arm, two-cohort multicenter study investigating the safety, tolerability, efficacy and pharmacokinetics of Prometic’s plasma derived IVIG in a total of 75 patients suffering from PIDD, including 50 adults (cohort 1) and 25 children (cohort 2).

PBP is currently developing and producing, for clinical trial and commercial launch purposes, plasma-derived protein therapeutics to address various medical conditions in both established and emerging markets. PBP’s Laval facility also serves as a conceptual blue print and training center for Prometic and its potential future partners PPPS™ based plasma purification plants.

In 2015, Prometic entered into a strategic manufacturing agreement with Emergent. The long-term manufacturing agreement provided Prometic with access to additional cGMP capacity in an FDA-licensed facility, located in Winnipeg, Canada. Prometic uses this capacity for the development and manufacture of plasma-derived biopharmaceuticals using Prometic’s proprietary plasma purification platform, Plasma Protein Purification System (PPPS™). In 2016, Prometic continued to tech-transfer and improve the efficiencies of this facility.

In 2015, the Corporation closed the acquisition of Emergent’s plasma collection center located in Winnipeg, Canada. The plasma collection center started to operate under Prometic’s ownership following the grant and receipt of the regulatory licenses by and from the requisite regulatory authorities. Prometic’s plasma collection center is an FDA and Health Canada licensed, EMA compliant and International Quality Plasma Program (iQPP) certified plasma collection facility conveniently located in close proximity to the existing Emergent Winnipeg based cGMP manufacturing facility. It allows for strategic sourcing of raw material for PPPS™ platform. It also allows PPR to use it as a blueprint to expand collection centers in Canada and in the USA. It allows for sale of plasma and blood products (i.e. RBCs). PPR is the entity responsible for securing Prometic’s plasma requirements necessary to extract the valuable proteins, which are currently under development, in clinical trials and in pre-commercialization phases. The plasma securing strategy is key to ensuring a steady reliable flow of raw material to be processed via Prometic’s PPPS™ purification technology. In 2016, PPR has focused on expanding its plasma donor base, upgrading its plasmapheresis equipment and the automation of certain SOPs. PPR is the first plasma collection company in Canada having expanded its Health Canada license to harmonize with US plasma collection regulations in order to be able to collect plasma two times per week per donor, thus increasing operational capacity. PPR successfully passed its US FDA regulatory inspection in 2016.

In 2016, Prometic closed the acquisition of Telesta. Prometic is currently evaluating the various options concerning Telesta’s manufacturing facilities in Belleville, Ontario and Montreal, Quebec with respect to their possible integration and use in the plasma-derived therapeutics business.



## ***Small-Molecule Therapeutics Segment***

For most of financial year ended December 31, 2016 (the “**2016 Financial Year**”), our subsidiary, Prometic Biosciences Inc. (“**PBI**”) operated the small molecule therapeutics development segment of our business. Following the SMIP corporate reorganization (mentioned in the December corporate highlights in section 6.2 of this AIF), PSMT now operates the small molecule therapeutics development segment of our business for the world (except Canada).

PBI has a strong pipeline of potential drug candidates. PBI scientists are focused on developing orally active drugs that provide, inter alia, competitive advantages including improved pharmaco-economics and safety profiles. Typically, these first-in-class therapeutics have efficacy and high-safety profiles confirmed in multiple pre-clinical experiments and early clinical trials and enjoy strong proprietary positions. The unmet medical applications targeted are in the fields of fibrosis which is implicated in a wide-range of major chronic diseases as well as many orphan ones (e.g. IPF), inflammation (e.g. diabetes), autoimmune diseases, oncology and hematopoietic disorders. As with its plasma-derived therapeutics division, Prometic is dedicated in becoming a strong integrated player in the orphan disease markets with its small-molecule therapeutics. See “Trends - Small-Molecule Therapeutics”.

With fibrosis affecting several different therapeutic areas, the business model for this segment is to consider commercializing the drug candidates for niche & rare diseases and partner promising drug candidates for medical conditions requiring significant marketing reach. While the Small Molecule Therapeutics Segment has several of such promising drug candidates, the Corporation has focused on working towards demonstrating that the positive data generated in several gold-standard animal models clearly indicating favorable effects in reducing the progression of fibrosis in various key organs would indeed translate to humans. PBI-4050 was found to be safe and very well tolerated without any serious adverse events in phase 1 clinical trial in 40 healthy volunteers and in 8 patients with chronic kidney disease. Three phase 2 open label clinical trials were then initiated. One multicenter trial in 40 patients with idiopathic pulmonary fibrosis, one trial in 24 patients with type 2 diabetes and metabolic syndrome (T2D&MS) in Canada and one in the UK in patients affected by Alström Syndrome (“**AS**”). In 2016 addition to PBI-4050’s safety and tolerability, Prometic also reported strong evidence of translation of pharmacologic activity in patients in these three trials. In fact, the pharmacological activity in T2D&MS patients was confirmed with a clinical and statistical significant reduction of glycated hemoglobin after 12 and 24 weeks of treatment along with a significant reduction of biomarkers associated to cardiovascular and renal injury. In addition, PBI-4050 demonstrated early evidence of efficacy in IPF patients whether used alone or in combination with one of the IPF approved drug. Finally, preliminary evidence of efficacy in reversing liver fibrosis in patients with AS treated with PBI-4050 was also observed.

There was no significant revenue derived from the Corporation’s Small Molecule Therapeutics Segment in the 2016 Financial Year and the financial year ended December 31, 2015 (the “**2015 Financial Year**”), respectively.

### **PBI-4050, Prometic’s Lead Compound**

PBI-4050 is currently the lead clinical compound targeting indications including Chronic Kidney Disease (“**CKD**”) associated with diabetes, Cystic Fibrosis and Related Diabetes and IPF. PBI-4050 is also targeting indications such as: multi-organ fibrosis and type 2 diabetes (Alström Syndrome), Metabolic Syndrome and type 2 diabetes and IPF.

### ***Fibrosis***

In 2016, PBI continued to focus activities to support additional orphan indications and to file additional patents for its anti-fibrotic drug candidates. Fibrosis is essentially scar tissue formation which occurs when an injury cannot be repaired with complete return to normal organ structure and function. The injury may simply be too severe (for example, a large skin wound) or may be chronic (for example diabetes,

viral hepatitis). Fibrosis may occur in any vital organ, and if progressive, lead to loss of organ function and death.

The proof of concept data generated to date in gold standard models confirms PBI's lead drug candidates' anti-fibrotic activity in several key organs including the kidneys, the heart, the lungs, the liver, the skin and the pancreas. Moreover, Prometic has been obtained results in knockout mice involving the two targeted receptors, confirming the involvement of these two receptors in fibrosis. Scientific manuscripts are currently in preparation for submission in recognized journals in 2017.

With the translation of pharmacological activity confirmed in humans with PBI-4050's performance in the 3 phase 2 open label trials, Prometic has also began the scale up of the manufacturing process for follow on drug candidates, namely PBI-4547 and PBI-4425. These follow-ons are analogues of PBI-4050 and have performed equally well in most animal models compared to PBI-4050, and in some cases, even outperformed PBI-4050. This provides Prometic with the ability to eventually position different drug candidates for different indications.

The quality of Prometic's R&D program and performance of its lead drug candidates to date has drawn the interest of leading medical experts. Several expert clinicians are now involved in the review of the data and the preparation of the clinical programs that would be required to secure regulatory approval for the targeted indications. While some unmet medical indications may not represent the highest value on a long term basis, the development strategy pursued may initially target smaller niche indications as a point of commercial entry before expanding to more lucrative medical uses.

Collaborators of PBI from Vanderbilt University, Ottawa University, l'Institut National de la Recherche Scientifique ("INRS") and the Montreal Heart Institute ("MHI") have continued to generate a large amount of positive data in 2016 in several gold-standard animal models confirming Prometic's own data and clearly indicating favorable effects in reducing the progression of fibrosis in various key organs. The data was presented at various prestigious industry conferences throughout the year.

Kidney: In collaboration with Drs. Thibodeau, Kennedy and Hébert from Ottawa University, both receptors targeted by PBI-4050 were localized in kidneys and were found to be overexpressed in various kidney diseases models. Furthermore, mice having deletion of these receptors showed some protection against fibrosis. Significant antifibrotic activity was confirmed in additional models of acute and chronic kidney injuries.

Pancreas: Additional experiments confirmed the potent anti-diabetic and anti-fibrotic activities of PBI-4050 and PBI-4547, in reducing blood glucose level and insulin resistance; and by improving kidney function in diabetic animal model. Both candidates, PBI-4050 and PBI-4547 have demonstrated strong protection of pancreatic and kidney functions in NOD (non-obese diabetic) mice, a model of Type 1 Diabetes.

Liver: PBI-4547 has demonstrated significant activity in reduction of liver steatosis and fibrosis in different models of obesity and NASH (nonalcoholic steatohepatitis) models.

Heart and lung: The Corporation also collaborates with scientists from the MCI to confirm cardioprotective effect of PBI-4050 originally observed in the 5/6 nephrectomized rat model. From these studies, under the supervision of Dr. Dupuis, results from early or late treatment with PBI-4050 showed very high efficacy in treatment of pulmonary hypertension and fibrosis after myocardial infarction in rat model.

### ***PBI-4050 Clinical Programs***

Prometic demonstrated that PBI-4050 was safe and well tolerated in its phase 1 clinical trial in 40 healthy volunteers followed by 8 patients with Chronic Kidney Disease. In both clinical trials no significant adverse events were noted, and the pharmacokinetic data validated our expectation of the once-daily oral dosing and the non-necessity to adjust dosage in patients with impaired renal function.

Two phase 2 CTAs were cleared by Health Canada in 2015. One is for an open-label study in patients with Type 2 diabetes with metabolic syndrome (“**T2D&MS**”) which commenced in Q1 2015, and the second is for an open-label study in patients with IPF, which commenced in Q2 2015. Another phase 2 open label study was also cleared in October 2015, this time for the treatment of patients with Alström Syndrome by the MHRA in the UK.

### ***Type 2 diabetes with metabolic syndrome (T2D&MS)***

On December 1st, 2015, Prometic reported that ten of the first eleven patients with T2D&MS, who had completed their 12-week treatment, had a reduction of their glycated hemoglobin (HbA1c). The average reduction was both clinically and statistically significant (-0.6% p=0.03), with such reduction exceeding 1% in some patients that had HbA1c level at screen greater than 7.5%. For instance, the 15 patients with a screening HbA1c  $\geq 7.5$  experienced a mean decrease of - 0.75% (p = 0.0004) while the 9 patients with a screening HbA1c  $\geq 8.0$ % experienced a mean decrease of - 0.9% (p = 0.007). The 10 patients who participated in the study’s 12 week extension had a mean HbA1c of 7.7 at screening and experienced a reduction of - 0.8% at week 12: this reduction was maintained at week 24. These results confirmed that pharmacological effect of PBI-405 translates to humans, and was achieved without any drug-related serious adverse events reported. Moreover, several biomarkers measured in blood or urine of patients and associated with a high incidence of cardiovascular complications and kidney injury when elevated in metabolic syndrome were significantly reduced by PBI-4050. In 2016, the Corporation decided to initiate a placebo-controlled phase 2 study in the same patient population with the objective to establish the optimal dose to achieve such beneficial effects. To this extent, this on-going clinical trial is expected to enroll 268 patients with T2D&MS and randomized in 4 arms: 1 placebo and 3 different doses.

### ***Idiopathic pulmonary fibrosis (IPF)***

For the phase 2 open label study in IPF patients, a total of 40 subjects enrolled in the study conducted in 6 sites across Canada and have completed the 12 weeks of treatment; 9 subjects received PBI-4050 alone, 16 received PBI-4050 & nintedanib and 15 received PBI-4050 & pirfenidone. The baseline characteristics of the subjects enrolled in this study were similar to those enrolled in prior IPF randomized controlled studies conducted by other pharmaceutical companies, namely ASCEND and INPULSIS.

In addition to demonstrating that PBI-4050 is safe and very well tolerated, an objective of this study was to seek early evidence of a clinical benefit with PBI-4050 treatment, whether administered alone or in addition to either of the drugs approved for the treatment of IPF, nintedanib or pirfenidone. On November 17, 2016, Prometic first reported on the first 30 subjects that completed 12 weeks of treatment.

PBI-4050, either used alone or in combination with one of the two drugs approved for the treatment of IPF (“**Combi-1**”), demonstrated very promising early indications of efficacy with the respiratory function of the subjects, measured as the forced vital capacity (FVC (ml)) which remained stable after 12 weeks of treatment. There were no serious adverse events requiring PBI-4050’s discontinuation. PBI-4050 was well tolerated whether used in combination or alone. With these positive results, the Corporation expects to initiate a placebo controlled, pivotal phase 2/3 IPF clinical trial in 2017.

Prometic held Pre-IND meeting with the FDA regarding PBI-4050 relating to IPF. During the Pre-IND meeting between Prometic and the lung division of the FDA for IPF, Prometic was advised to proceed with a phase 2/3 pivotal clinical trial that would evaluate the add-on effect of PBI-4050 to the current standard of care in the USA. The positive results observed in the phase 2 open label trial with PBI-4050 used alone or in combination with one of the two IPF drugs will enable Prometic to adjust the design of the pivotal clinical trial accordingly.

### ***Chronic Kidney Disease (CKD)***

Prometic held Pre-IND meeting with the FDA regarding PBI-4050 relating to CKD. Prometic met with the Cardiovascular and Renal Division of the FDA, focused on Prometic’s proposed phase 2/3 clinical

program, for PBI-4050, in patients with CKD with diabetes was followed by another pre IND meeting, this time with both the Cardiovascular and Renal Division and the division of metabolism and endocrinology products (DMEP). The main purpose was to discuss the impact on the positive results obtained in the phase 2 trial in T2D&MS patients on the proposed design of the phase 2/3 trial and end points.

### ***Alström syndrome (AS)***

The clinical trial in AS patients is a very challenging test of the efficacy of PBI-4050. AS is a rare inherited autosomal recessive syndrome characterized by the onset of obesity in childhood or adolescence, Type 2 diabetes with severe insulin resistance, dyslipidemia, hypertension and severe multi-organ fibrosis, involving the liver, kidney and heart. AS is also characterized by a progressive loss of vision and hearing, a form of heart disease that enlarges and weakens the heart muscle (dilated cardiomyopathy), and short stature. This disorder can also cause serious or life-threatening medical problems involving the liver, kidneys, bladder, and lungs.

The progression of liver fibrosis is much more aggressive in patients with AS than in “typical” metabolic syndrome patients with obesity, diabetes and fatty liver. Non-alcoholic fatty liver disease (“**NAFLD**”) is the manifestation of metabolic syndrome in the liver. Due to the worldwide obesity epidemic, NAFLD now affects 20–30% of the general population and thus has become by far the most common cause of chronic liver disease. Preliminary results in AS patients indicated a reduction of elevated liver enzymes and a reduction of fibroscan® scores, which suggest PBI-4050 pharmacologic effect on their liver.

The on-going study is an open-label, single-arm, phase 2 trial initially recruiting up to 20 patients. Each patient will be evaluated against their respective baseline, given the severity of their medical conditions. The initial treatment period is 6 months with a possibility to extend the study. The objectives of the study are to evaluate the safety and tolerability of PBI-4050, and the effects of PBI-4050 on key organ functions, disease progression and inflammatory/fibrotic markers.

In addition to the Orphan Drug Designation for the IPF indication granted for PBI-4050 by the FDA and EMA for the USA and Europe respectively in 2015, an ODD was also granted by the FDA for PBI-4050 for the AS indication.

### ***Other Drug Candidates to Treat Fibrosis Related Diseases***

Prometic is currently reviewing various strategic avenues to further advance its most promising lead drug candidates in the clinics. PBI-4050 is prioritized, followed by PBI-4547, PBI-4425, PBI-4419 and other analogs. The manufacturing processes for both PBI-4547 and PBI-4425 are being scaled up to enable the commencement of their respective clinical program. Both compounds performed equally well compared to PBI-4050 in most preclinical models and have outperformed PBI-4050 in some models. This provides Prometic with the opportunity to specifically target specific indications with these two drug candidates and expand commercial & partnering opportunities. See “Commercial Applications, Products and Services”.

### ***Other Drug Candidates to Treat Auto-Immune Diseases***

Additional drug candidates such as PBI-1737 and PBI-1308 offer the potential to treat various auto-immune diseases such as ulcerative colitis, lupus, and rheumatoid arthritis. These drug candidates are at an advanced pre-clinical stage, with preliminary toxicology data supporting the view that they may represent a well-tolerated and safe treatment for patients affected by such conditions.

The Corporation intends to fund the development program for the above mentioned compounds via a combination of avenues including: funds generated by the bioseparations division as well as plasma-derived therapeutics business segments; funding achieved through strategic partnering with other pharmaceutical companies; and funding via financial partnerships or equity or debt funding initiatives.

## 6.2. Trends

### **Protein Technologies Segment**

#### *Bioseparation Technologies*

Recombinant proteins, unlike their human plasma counterparts, are produced in non-human hosts and undergo intensive purification to remove host cell-derived impurities. Monoclonal antibodies (MAbs), represent approximately 40% of the recombinant protein market and the global monoclonal antibody market size exceeded \$85.4 billion in 2015<sup>1</sup>. Other proteins in the recombinant protein market include growth factors, cytokines, hormones, fusion proteins, blood factors, vaccines, and therapeutic enzymes. The global market for biologics in 2013 was \$200.6 billion and is anticipated to reach \$387 billion in 2019<sup>2</sup>. The global market for bioseparation products is expected to grow from \$3.25 billion in 2012 to \$6 billion in 2018 at a compound annual rate of 11%. In 2013 the market for bioseparation systems was anticipated to exceed \$3.6 billion which includes chromatography with a market value of \$1.8 billion<sup>3</sup>.

#### *Plasma-Derived Therapeutics (Biologics)*

Plasma is the protein fluid component of blood that remains once the red cells, white cells, and platelets have been removed. The global market for plasma-derived products is both fast growing and lucrative and generated in excess of USD\$19.7 billion in 2015<sup>4</sup>. While the majority of revenue comes from Europe and North America, management estimates that demand from emerging markets, and particularly within Asia & Pacific region, will grow rapidly in the coming years. There is a growing demand and a shortage of supply for high value plasma proteins commonly used to treat a variety of medical conditions.

### **Small-Molecule Therapeutics Segment**

**Chronic Kidney Diseases.** In 2014, approximately 30.4 million people in the USA were diagnosed with chronic kidney diseases<sup>5</sup>. Fibrosis is the main mechanism via which the condition of CKD patients deteriorates, leading to further loss of renal function, increased cardiovascular complications, and eventually, the need for dialysis treatment while waiting for a kidney transplant. Patients diagnosed with severe CKD stages (3 and 4) often suffer from a gradual and accelerated loss of their renal function (end-stage renal disease or ESRD) leading to the need for hemodialysis. Cardiovascular complications for ESRD patients on hemodialysis are a common cause of death.

Diabetic nephropathy is a complication of long-standing diabetes mellitus, of both Type 1 and Type 2. It is increasing in incidence throughout the world, and in many countries, including the USA and Canada, is the leading cause of end-stage renal disease requiring maintenance dialysis and/or kidney transplantation.

**Metabolic Syndrome and Resulting Type II Diabetes.** Metabolic syndrome is a major risk factor for cardiovascular disease and for Type 2 diabetes, and consists of the constellation of central (truncal) obesity, high blood triglycerides, low HDL (“good”) cholesterol, elevated blood pressure, and elevated blood glucose. Obesity is believed to cause a chronic inflammatory state, which leads to insulin resistance and so may in turn result in cardiovascular disease and/or Type 2 diabetes. Given the global epidemic of obesity, both in the developed and developing world, metabolic syndrome and its consequences present a devastating public health problem. It is difficult to grasp the numbers and the overwhelming public health issues presented by the global epidemic of obesity, metabolic syndrome, and

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<sup>1</sup> GrandView Research, Monoclonal Antibodies (mAbs) Market Analysis By Source, November 2016.

<sup>2</sup> Biologic Therapeutic Drugs; Technologies & Global Markets, BCC Research, January 2015.

<sup>3</sup> Bioseparation Systems for Global Biopharmaceutical Markets, Trimark Publications LLC, August 2013.

<sup>4</sup> The Marketing Research Bureau, Inc., The Worldwide Plasma Proteins Market 2014

<sup>5</sup> 2016 annual data report from the United States Renal Data System.

Type 2 diabetes. The International Diabetes Federation estimates that in 2015, there were 415 million adult diabetics worldwide, and expects that number to increase to 642 million by the year 2040. The Centers for Disease Control estimates that 1 out of 3 children born in the USA during the year 2000 will develop diabetes during their lifetime<sup>6</sup>.

**Idiopathic Pulmonary Fibrosis.** Idiopathic pulmonary fibrosis is a chronic and fatal disease characterized by a progressive decline in lung function. It is a specific type of interstitial lung disease in which the small air sacs of the lung, the “alveoli”, gradually become replaced by fibrotic (scar) tissue and is the cause of worsening dyspnea (shortness of breath). IPF is usually associated with a poor prognosis. The term “idiopathic” is used because the cause of pulmonary fibrosis is unknown. IPF usually occurs in adult individuals of between 50 and 70 years of age, particularly those with a history of cigarette smoking, and affects men more than women. IPF affects about 130,000 people in the USA, with about 48,000 new cases diagnosed annually. Approximately 40,000 people die each year with IPF. The 5-year mortality rate for patients with IPF is estimated to range from 50% to 70%<sup>7</sup>.

**Orphan or Rare Diseases<sup>8</sup>.** Rare diseases is currently one of the most rapidly expanding areas of research and clinical development. It is estimated that there are approximately 7,000 to 8,000 rare diseases worldwide already identified, with approximately 250 new rare diseases identified annually. In addition, it is estimated that rare diseases are affecting more than 25 million people in the USA, more than 55 million people in the USA and EU combined; or approximately 10% of all people worldwide. An orphan or rare disease is normally defined by less than 200,000 patients in the USA<sup>9</sup>, less than 250,000 patients in the EU<sup>10</sup> and less than 50,000 patients in Japan<sup>11</sup>. The commercial incentives granted for such designation usually include 7 years of marketing exclusivity from approval in the USA<sup>12</sup> and 10 years of marketing exclusivity from approval in the EU<sup>13</sup>. There are also other financial incentives via reduced R&D costs, grants for phase 1 to phase 3 clinical trials and waived user fees. It is estimated that prescriptions for orphan drugs will achieve a compound annual growth rate (CAGR) of 11.1% in the period from 2015 to 2020, almost double the overall prescription market growth rate. Orphan drug sales are forecast to reach approximately \$209 billion worldwide by 2022, representing just over 21% of the entire global prescription drug market (excluding generics).

**Cystic Fibrosis-Related Diabetes** - Cystic fibrosis (CF) is a life-threatening, genetic disease that affects especially the lungs but also the pancreas, liver, kidneys, and gut. Damage to the pancreas can lead to loss of the islet cells, leading to a type of diabetes that is unique to those with the disease. This cystic fibrosis-related diabetes (“CFRD”) shares characteristics that can be found in type 1 and type 2 diabetics without CF, and is one of the principal non-pulmonary CF related complications. CFRD increases in prevalence with increasing age, and is becoming more common as the life expectancy of patients with CF improves, and is now the most common non-respiratory complication of CF. According to the Cystic Fibrosis Foundation, a total of 70,000 people in the USA and Europe suffer from cystic fibrosis of which more than 70% are CFRD by the age of 20<sup>14</sup>. There are two FDA approved drugs for the treatment of CF targeting a select segment of the population, which together generated revenues of US\$1.7bn in 2016 but none for CFRD. We believe this unmet medical need could represent a substantial opportunity.

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<sup>6</sup> [www.idf.org/diabetesatlas/update-2014](http://www.idf.org/diabetesatlas/update-2014)

<sup>7</sup> [www.coalitionforpfp.org/facts-about-idiopathic-pulmonary-fibrosis/](http://www.coalitionforpfp.org/facts-about-idiopathic-pulmonary-fibrosis/)

<sup>8</sup> Orphan Drug Report 2017, EvaluatePharma®, February 2017.

<sup>9</sup> <http://www.fda.gov/Drugs/ResourcesForYou/Consumers/ucm143563.htm>

<sup>10</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/special\\_topics/general/general\\_content\\_000034.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/general/general_content_000034.jsp)

<sup>11</sup> [http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/orphan\\_drug.html](http://www.mhlw.go.jp/english/policy/health-medical/pharmaceuticals/orphan_drug.html)

<sup>12</sup> <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107293.htm#>

<sup>13</sup> [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000393.jsp](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000393.jsp)

<sup>14</sup> CFRD The Next Challenge, Yves Berthiaume, IRCM, 2015

### 6.3. Objectives and R&D

#### ***Protein Technologies Segment***

##### *Bioseparation Technologies*

Partnership and joint-venture agreements concluded over the past decade have enabled Prometic to position itself as a key player in the biopharmaceutical purification market. In creating such relationships, the Corporation's goal is to maximizing its value, all the while obtaining significant third party endorsement of Prometic's technology. Once again, for the coming year, Prometic intends to increase its customer base for its bioseparation products and services and to partner with pharmaceutical and biopharmaceutical companies to improve the manufacturing of their own therapeutics. Moreover, Prometic intends to focus on its R&D and technical support programs to complement the technology transfer initiatives of PBT for implementing of PPPS™ technology at larger scales for Prometic's use. Further Prometic continues to expand its resin manufacturing capabilities due to expected increase demand as PPPS™ products obtain regulatory approval.

The Corporation intends to continue to develop and improve its affinity resins to be implemented in the PPPS process and provide regulatory support to all customers of said resins as well as other non-PPPS™ related absorbents.

##### *Plasma-Derived Protein Therapeutics (Biologics)*

Over the years, Prometic has evolved from solely being a provider of enabling manufacturing technologies to third party pharmaceutical companies to becoming a fully integrated biopharmaceutical company leveraging the same proven technologies such as PPPS™ to develop its own pipeline of plasma derived-therapeutics.

Prometic continues to invest in R&D activities in the plasma-derived therapeutics field with a primary focus on both unmet medical needs and orphan indications such as plasminogen as well as well-established and growing markets (e.g. IVIG) where we can capitalize on our plasma protein extraction yield advantage. The former type of products are pursued with a view to provide additional economics and cost savings from the processing of plasma for the orphan therapeutics. In 2016, Prometic continued its efforts to expand the potential clinical indications of its first drug candidate, plasminogen. In fact, Prometic had entered into a strategic agreement with Omnio in November 2015 to do so. That agreement provided Prometic with an exclusive intellectual property license as well as a comprehensive proprietary understanding of the use of plasminogen in the field of hard-to-treat wounds. Prometic secured exclusive license rights to both issued and pending patents for the use of plasminogen related to wound healing. The deal enabled Prometic to access extensive preclinical data as well as unique proof of concept efficacy data in patients. Hard-to-treat wounds such as diabetic foot ulcers affect millions of patients in the USA and represent annual incremental healthcare costs as high as US\$13 Billion. Studies have indicated that diabetics have a lifetime risk as high as 25% of developing foot ulcers and annual incident cases are cited to range from 1% to 4.1%. Since then, Prometic has filed several patent applications regarding plasminogen's use and formulations to protect other clinical indications. In 2016, Prometic announced that it would be pursuing tympanic membrane perforations ("TMP"), as one of its new plasma-derived plasminogen targeted clinical indications.

Securing and refurbishing the Laval plant operated by PBP over the last couple of years and implementing the PPPS™ process in the Emergent facility has enabled the Corporation to begin implementing its PPPS™ process in-house and manufacture current GMP grade products for Prometic's clinical trial and eventual commercial needs.

In 2016, Prometic acquired Telesta which possessed GMP manufacturing facilities. Prometic is currently evaluating the various options concerning Telesta's manufacturing facilities in Belleville, Ontario and

Montreal, Quebec with respect to their possible integration and use in improving efficiencies and further consolidating its plasma-derived therapeutics manufacturing and business activities.

In 2015, the Corporation closed the acquisition of Emergent's plasma collection center located in Winnipeg, Canada. The plasma collection center started to operate under Prometic's ownership following the grant and receipt of the regulatory licenses by and from the requisite regulatory authorities. Prometic's plasma collection center is an FDA and Health Canada licensed, EMA compliant and International Quality Plasma Program (iQPP) certified plasma collection facility conveniently located in close proximity to the existing Emergent Winnipeg based cGMP manufacturing facility. It allows for strategic sourcing of raw material for PPPS™ platform. It also allows PPR to use it as a blueprint to expand collection centers in Canada and in the USA. It allows for sale of plasma and blood products (i.e. RBCs). PPR is the entity responsible for securing Prometic's plasma requirements necessary to extract the valuable proteins, which are currently under development, in clinical trials and in pre-commercialization phases. The plasma securing strategy is key to ensuring a steady reliable flow of raw material to be processed via Prometic's PPPS™ purification technology. In 2016, PPR has focused on expanding its plasma donor base, upgrading its plasmapheresis equipment and the automation of certain SOPs. PPR is the first plasma collection company in Canada having expanded its Health Canada license to harmonize with US plasma collection regulations in order to be able to collect plasma two times per week per donor, thus increasing operational capacity. PPR successfully passed its US FDA regulatory inspection in 2016.

### ***Small Molecule Therapeutics Segment***

The Corporation has focused on the clinical advancement of its lead therapeutic compound, PBI-4050, both for orphan indications such as IPF, AS and Cystic Fibrosis as well as for large fibrosis related indications such as CKD and inflammation related diseases such as metabolic syndrome & type 2 diabetes. See "PBI-4050, Prometic's Lead Compound". The Corporation is developing analogs and derivatives of PBI-4050 such as PBI-4547, PBI-4425 and PBI-4419 which have performed equally well in preclinical models and in some instances, outperformed PBI-4050 for certain indications. As evidence of clinical efficacy is demonstrated with PBI-4050 in phase 2 clinical trials, some indications originally targeted for PBI-4050 could be allocated to such analogues. For these reasons, future indications such as scleroderma could be allocated to PBI-4425, while PBI-4547 could be allocated to NASH. The Corporation continues to develop its pipeline of drug candidates in the fields on autoimmune disease (e.g. PBI-1308 and PBI-1737) and hematology (e.g. PBI-1402).

Further, with respect to its small molecule therapeutics, the Corporation has focused on the development of a pipeline of potentially valuable compounds which it intends to ultimately license or partner at the appropriate stage of development. It is generally not Prometic's intention to undertake late-stage clinical trials (phase 3) in large indications (like DKD) without the support of a strategic venture or big pharma partner. Prometic may pursue smaller niche orphan indications on its own.

Prometic generally conducts R&D through its own scientific staff, though in some cases it coordinates discrete R&D tasks carried out by third parties or carries out certain R&D activities in collaboration with commercial or academic partners.

## **6.4. Commercial Applications, Products and Services**

The Corporation currently has a number of partnerships that generate revenues and increase the use of its products and technologies and bioseparation media. Additionally, the Corporation has benefits from royalty and milestone payments from products sold by partners who have the right to use the Corporation's technology in their manufacturing processes. The Corporation also benefits from licensing of its technology platform and by sharing clinical development and marketing risks through these partnerships. Additionally, the Corporation receives service fees, contributing to covering some of the costs of current operations, allowing for further product growth and expansion. Finally, the Corporation



continues to ensure that its product supply capacity is ready to serve its affiliates needs as proprietary therapeutics advance through the clinics and eventually receive regulatory approval for sale.

Whilst Prometic expects to continue generating some service revenues and revenues from partnering with strategic third parties for the development and use of its key products and assets, in the short-term, the Corporation expects to focus on ensuring that additional plasma-derived and small-molecule therapeutics start entering clinical development stages. As such, Prometic anticipates the filing of additional IND applications to take place during the financial year ended December 31, 2017. The Corporation will also continue to pursue the development of other therapeutics (both plasma-derived and small molecule) in their clinical development stages as well as filing INDs for various new indications to be treated with plasminogen. The filing of such INDs and continued pursuit and advancement of clinical trials in patients is perceived by management to be value creation events since such actions mark the entering in the regulatory approval process.

The Corporation also intends to exploit the operational benefits derived from launch of its plasma purification facility and the expansion into Emergent's facility for the supply of clinical trial material and for the eventual commercial launch of its first plasma-derived product, plasminogen, in order to prepare for additional plasma-derived products for upcoming IND filings to ensure a constant flow of movement and progress in the development of Prometic's product pipeline.

Finally, Prometic is preparing for the expected commercial launch of its first plasma-derived therapeutic, plasminogen for which a rolling BLA filing has commenced.

### ***Protein Technologies Segment***

#### ***Bioseparation Technologies***

Prometic's innovations in the area of bioseparation technologies have created three potential revenue paths: (i) sale of bioseparation products and services, (ii) development and out-licensing of purification technology to drug manufacturers; and (iii) licensing and supply of technology for use in the manufacture of safer blood-derived products.

Prometic's bioseparation technologies and products enable the purification of biopharmaceuticals and assist in their efficient manufacture. At least 14 different products developed by our customers and licensees with the assistance of Prometic's purification technologies have been approved by regulatory bodies thus far, including the EMA and FDA. These customers and licensees are well-known names in the pharmaceutical and biopharmaceutical industries. As the R&D and manufacturing activities of Prometic's clients increase, Prometic expects product sales to increase and for additional new products to enter the market. Management believes the Corporation is well-positioned to meet this demand by virtue of the strategic investments it has made in its production facilities. This evolution represents important growth and an established expanding revenue stream for Prometic.

Prometic believes that as it and its various partners implement its PPPS™ process, this will increase the need for Prometic's bioseparation products. Prometic believes that PPPS™ platform-based facilities such as the Laval facility, Emergent facility and MasterPlasma LLC facility will increase the number of products being eventually approved, having been manufactured, in part, using the bioseparation technology.

#### ***Plasma-Derived Protein Therapeutics (Biologicals)***

Prometic's innovations in the area of purification of plasma-derived therapeutics have created commercial avenues. While the future revenues arising from the partnering and licensing of the technology in emerging or closed markets such as China remain of interest to Prometic, revenues relating to the selling of PPPS™ therapeutics for its own benefit are expected to be far more substantial.

The potential benefits of Prometic's protein extraction technologies are being increasingly recognized worldwide. Manufacturers of drugs derived from plasma can achieve higher yields and more efficient

processing through the use of Prometic's PPPS™. At the same time, the Corporation intends to leverage its technology not only to generate licensing revenues (e.g. Wuhan license), but more importantly focusing on its own manufacturing and product commercialization revenues.

During the 2016 Financial Year, Prometic number one focus was the successful completion of the plasminogen clinical trial, on the commencement of the filing of its rolling BLA and on the preparation for commercial product launch in 2017. This was closely followed by the advancement of other plasma derived therapeutics such as IVIG and eventually other proteins such as Alpha1 Antitrypsin (A1PI) and interalpha1 inhibitor protein (IAIP).

Prometic is currently evaluating the various options concerning Telesta's manufacturing facilities in Belleville, Ontario and Montreal, Quebec with respect to their possible integration and use in plasma-derived therapeutics business.

In 2015, the Corporation closed the acquisition of Emergent's plasma collection center located in Winnipeg, Canada. The plasma collection center started to operate under Prometic's ownership following the grant and receipt of the regulatory licenses by and from the requisite regulatory authorities. Prometic's plasma collection center is an FDA and Health Canada licensed, EMA compliant and International Quality Plasma Program (iQPP) certified plasma collection facility conveniently located in close proximity to the existing Emergent Winnipeg based cGMP manufacturing facility. It allows for strategic sourcing of raw material for PPPS™ platform. It also allows PPR to use it as a blueprint to expand collection centers in Canada and in the USA. It allows for sale of plasma and blood products (i.e. RBCs). PPR is the entity responsible for securing Prometic's plasma requirements necessary to extract the valuable proteins, which are currently under development, in clinical trials and in pre-commercialization phases. The plasma securing strategy is key to ensuring a steady reliable flow of raw material to be processed via Prometic's PPPS™ purification technology. In 2016, PPR has focused on expanding its plasma donor base, upgrading its plasmapheresis equipment and the automation of certain SOPs. PPR is the first plasma collection company in Canada having expanded its Health Canada license to harmonize with US plasma collection regulations in order to be able to collect plasma two times per week per donor, thus increasing operational capacity. PPR successfully passed its US FDA regulatory inspection in 2016.

The following table indicates, for each of the two most recently completed financial years, the revenues for each category of products or services that accounted for 15% or more of the Corporation's total consolidated revenues for the applicable financial year derived from sales to third party customers by the Corporation's Protein Technologies Segment combined:

Protein Technologies Segment Combined Revenues		
Financial Year	2016 Financial Year*	2015 Financial Year**
Services	\$3.4 million	\$1.8 million
Resins Sales	\$12.9 million	\$21.4 million
Milestone and licensing revenues	0	\$1.3 million

\* The foreign exchange rates applicable, from GBP to CAD = 1.8072 and from USD to CAD = 1.3377

\*\* The foreign exchange rates applicable, from GBP to CAD = 1.9892 and from USD to CAD = 1.3174

## Small Molecule Therapeutics Segment

Prometic is working towards the development of the small molecule therapeutic unit with a pipeline of compounds in diverse medical indications, as summarized in the table below:

Prometic Compound	Indications
PBI-4050	<ul style="list-style-type: none"><li>○ Cystic Fibrosis and Related Diabetes</li><li>○ Diabetic kidney disease (DKD)</li><li>○ Chronic kidney disease (CKD)</li><li>○ Idiopathic pulmonary fibrosis (IPF)</li></ul>
PBI-4050	Other multi-organ fibrosis-related diseases and rare diseases (e.g. Alström Syndrome, scleroderma)
PBI-4547	<ul style="list-style-type: none"><li>○ Diabetes</li><li>○ NASH</li></ul>
PBI-4425	<ul style="list-style-type: none"><li>○ IPF</li><li>○ Scleroderma</li></ul>
PBI-4419	Osteoporosis and Cancer
PBI-1402	Anemia and Cancer
PBI-1737 and PBI-1308	Various auto-immune diseases such as: <ul style="list-style-type: none"><li>○ ulcerative colitis</li><li>○ lupus; and</li><li>○ rheumatoid arthritis</li></ul>

**Fibrosis (PBI-4050).** By reducing the level of fibrosis in tissues/organs such as kidney, lung, heart, liver and pancreas, Prometic's therapeutics could offer the prospect of delaying the progression of various fibrosis-related diseases, such as kidney diseases (CKD, DKD, ESRD (end stage renal disease), IPF, heart (reduction in post-myocardial infarction), liver (NASH) and diabetes (reduction of insulin resistance and pancreatic fibrosis). and overall improving greatly the quality of life of patients while reducing significantly the costs to the healthcare system.

**Oncology.** PBI-1737 has been shown to display significant anti-tumor activity both in vitro and in vivo. Pre-clinical data for compound PBI-4419 demonstrated anti-cancer activity in the mouse (P815) mastocytoma model. Data on PBI-1308 demonstrated a reduction of inflammation and cancer cell proliferation through inhibition of the NF- $\kappa$ B transcription complex in prostate cancer.

**Autoimmune.** PBI-1737 and PBI-1308 also offer the potential to treat various autoimmune diseases such as ulcerative colitis, lupus, and rheumatoid arthritis.

**Osteoporosis.** PBI-4419 has been shown to reduce osteoporosis in an ovariectomized-rat model mimicking post-menopausal osteoporosis.

**Anemia.** PBI-1402 has been shown to reduce blood transfusion in chemotherapy-induced anemia.

Priority has been given to the various anti-fibrotic indications of PBI-4050. Should additional R&D financing becomes available for advancement of the other compounds, these compounds could represent important pipeline additions to the Corporation's lead clinical drug candidates.

## **6.5. Competitive Conditions**

The biopharmaceutical industry is extremely competitive. Prometic competes with companies that produce similar or identical biopharmaceutical products or that propose different approaches to the separation or purification of proteins. Many such companies have greater resources than Prometic. Accordingly, no assurance can be given that products developed by these other companies or that their equivalent technology will not affect Prometic's competitiveness.

Management believes Prometic's competitive edge resides in the following: its ability to apply its technologies to a wide range of products already on the market; the ability of its technology to improve the manufacturing of these products through product yield increases and safety or cost improvements; the ability to apply its technology in many other areas such as drug discovery, proteomics, diagnostics, blood safety; the possibility of establishing a solid base to drive revenue growth; leveraging its expertise in protein mimetics and medicinal chemistry to develop and build on an established pipeline of therapeutic products that target unmet medical needs where standard therapies are either in limited supply or economically burdensome.

## **6.6. Raw Materials, Components**

Prometic mostly depends on third parties for the sourcing of raw materials, components or finished products for Prometic's various products. Prometic believes that alternative sources of supply for such raw materials, components or finished products exist. However, any change in Prometic's suppliers could have a significant impact on Prometic's ability to complete certain projects and, accordingly, would affect its projected commercial and financial growth. While other potential alternative suppliers of raw materials and components have been identified or are being determined, they must first pass intensive validation tests to ensure their compliance with product specifications. No assurance can be given regarding the successful outcomes of such tests or the ability of Prometic to secure alternate sources of supply at competitive pricing.

## **6.7. Intellectual Property Rights**

Prometic's success depends in part on its ability to obtain patents, protect its trade secrets and operate without infringing third-party exclusive rights or without others infringing Prometic's exclusive rights or those granted to it under license. Prometic has filed patent applications in Canada, the USA, Europe and elsewhere in the world and is actively pursuing these matters. The patent position of biopharmaceutical firms is generally uncertain and involves complex legal, factual and scientific issues, several of which remain unresolved. The Corporation does not know whether any of Prometic's pending patent applications will be granted or whether Prometic will be able to develop other patentable proprietary products. Furthermore, Prometic does not know whether its existing or future patents will provide a competitive advantage or afford protection against competitors with similar technology. In addition, the Corporation cannot give any assurance that such patents will not be challenged successfully or circumvented by others using alternative technology or whether existing third-party patents will prevent Prometic from marketing its products. Finally, competitors or potential competitors may independently develop products as effective as those of Prometic or invent other products based on Prometic's patented products.

Pharmaceutical and biopharmaceutical companies and R&D and academic institutions may have filed patent applications for processes related to those of Prometic and which may have an effect on its business. Such processes may conflict with Prometic's processes or patent applications, which could limit the scope of the patents that may be granted to Prometic or even result in its patent applications being rejected.

If third-party licenses are required, there can be no assurance that Prometic will be able to obtain such licenses, or if obtainable, that it would be available on reasonable terms. Furthermore there can be no

assurance that Prometic could develop or obtain alternative technologies related to third party patents that may cover its products. The inability to obtain such licenses or alternative technologies could delay the market launch of certain Prometic products, or even prevent Prometic from developing, manufacturing or selling certain products. In addition, Prometic could incur significant costs in defending itself in patent infringement proceedings initiated against it or in bringing infringement proceedings against others.

Prometic cannot determine with any certainty if it has priority of invention in relation to a product or process covered by a patent application or if it was the first to file a patent application for any such invention. Further, in the event of patent litigation there can be no assurance that Prometic's patents, if issued, would be held valid or enforceable by a court of competent jurisdiction or that a court would rule that the competitor's products or technologies constitute patent infringement.

Moreover, a significant part of Prometic's technological know-how constitutes trade secrets. Prometic, therefore, requires that its employees, consultants, advisers and collaborators as well as strategic partners and licences sign confidentiality agreements. However, there can be no assurance that such agreements provide adequate protection in the event of unauthorized use or disclosure of Prometic's trade secrets, know-how or other proprietary information.

### **6.8. Product Development**

Prometic currently has a number of collaboration agreements based on its technology for the improvement of established and marketed therapies by improving manufacturing process yield and purity, and by developing recombinant versions of established proteins. Prometic also leverages its expertise in protein therapeutics and medicinal chemistry and has accumulated an impressive pipeline of therapeutic product candidates for which the development is conducted in-house. Prometic believes it is important to maintain a balance between in-house product development products and partnered products. Developing products internally provides greater control over the pace of development and the potential for higher commercial returns. Furthermore, it allows Prometic to develop the necessary skill sets as it drives toward its goal of becoming a fully integrated specialty pharmaceutical company. Pursuing the commercialization phase in partnership with other firms is also important for the Corporation because it provides continuous external validation of Prometic's technology and possibilities of short and long term revenues from fees collected at the initiation of the partnership as well as via milestones payments and royalty streams.

### **6.9. Research and Development**

Prometic's policy for R&D is to have readily available funds to conduct its activities. Prometic's strategy is to finance its research activities through the formation of strategic alliances with pharmaceutical and biopharmaceutical companies, debt and equity, financings as well as grants or R&D tax credits for such purposes. During the course of the 2016 Financial Year, Prometic invested approximately \$89.7 million in R&D, of which \$1.7 million were refundable.

### **6.10. Environmental Protection**

Prometic produces a certain amount of chemical waste in its R&D and manufacturing activities that is removed in accordance with applicable environmental protection standards by companies that specialize in hazardous waste management. Prometic's research laboratories generate radioactive waste that is also removed by companies that specialize in hazardous waste management, in accordance with strict internal procedures and applicable regulatory requirements. Compliance with such requirements is not expected to have a significant effect on Prometic's competitive position or to have a significant effect in future years.

## 6.11. Employees

Prometic has highly-qualified employees with specialized backgrounds in the biological and chemical sciences. The Corporation leverages the fact that many scientists and managers within multinationals work on joint projects with Prometic. These relationships enables Prometic to gain access to an extended knowledge base. Prometic has also recruited experienced professionals in the area of business development, finance, marketing, clinical/regulatory, accounting, human resources and drug manufacturing. On a consolidated basis as at December 31, 2016, Prometic had 389 employees in research and production facilities in Canada, the USA, the Isle of Man and the UK as well as marketing and project management presence in the USA, Europe and Asia. Further, Prometic complements its work force with experienced consultants in various relevant fields.

## 7. RISKS AND UNCERTAINTIES RELATED TO PROMETIC'S BUSINESS

Investors should consider the following risk factors, which are inherent to the Corporation and affect its business, and other information contained in this Annual Information Form, before deciding to purchase securities of the Corporation. If any of the following risks occur, the business, financial condition and operating results of Prometic could be adversely affected. As a result, the trading price of the Corporation's securities could decline and investors could lose part or all of their investment.

The risks and uncertainties described below are those we currently believe to be material, but they are not the only ones we face. If any of the following risks, or any other risks and uncertainties that we have not yet identified or that we currently consider not to be material, actually occur or become material risks, our business, prospects, financial condition, results of operations and cash flows and consequently the price of the Common Shares could be materially and adversely affected. In all these cases, the trading price of the Common Shares could decline, and you could lose all or part of your investment. There is no assurance that risk management steps taken will avoid future loss due to the uncertainties described below or other unforeseen risks.

***The commercial success of the Corporation depends largely on the development and commercialization of its products derived from its Small Molecule Therapeutics Segment and the successful execution on the development and commercialization of its products derived from its Protein Technologies Segment.***

The commercial success of the Corporation depends largely on the development and commercialization of its products derived from its Small Molecule Therapeutics Segment and the successful execution on the development and commercialization of its products derived from its Protein Technologies Segment. The failure by the Corporation to do so will have a material adverse effect on the Corporation. The Corporation's focus in its small molecule therapeutics' has been on development and partnering activities for PBI-4050 and/or analogs thereof in which it has invested a significant portion of its financial resources and time. Although the Corporation has other compounds and analogs, most are at an earlier stage of development.

The Corporation's focus on its Protein Technologies Segment has been to develop and commercialize products related to the bioseparation, pathogen reduction and human plasma-derived therapeutics.

The ability of the Corporation to generate revenues in the future is primarily dependent on the partnering of its compounds and/or its analogs in its Small Molecule Therapeutics' Segment, the successful execution on license agreements and other forms of agreements that are already in place, and execution on additional new license agreements and other form of commercialization agreements for its Protein Technologies division such as long-term supply agreements. There can be no guarantees that any of its compounds will be commercialized since they are still under development. Also, there can be no guarantee of commercialization of these compounds since they will depend on several factors:

- successful completion of clinical trials;
- timely receipt of regulatory approvals from the FDA and other regulatory agencies;
- market acceptance of the product by the medical community, patients and third-party payers (such as governmental health administration authorities and private health coverage insurers);
- successful marketing and sales force or the entering into a commercial agreement with a partner to help the marketing and sale of the compounds;
- maintaining of manufacturing and supply agreements in place to ensure commercial quantities of the compounds through validated processes;
- an increase in the number of competitors in the same market;
- ability for the Corporation to effectively protect his intellectual property and avoid patent infringement; and
- any other condition, obligation or requirement that may arise, all of which may delay the Corporation's capacity to generate revenues and will adversely materially affect its financial conditions and operating results.

***The Corporation does not have the required regulatory approval to commercialize its products and cannot guarantee that it will obtain such regulatory approval.***

The Corporation does not have the required regulatory approval to commercialize its products and cannot guarantee that it will obtain such regulatory approval. The commercialization of the Corporation's products first requires the approval of the regulatory agencies in each of the countries where it intends to sell its products. In order to obtain the required approvals, the Corporation must demonstrate, following preclinical and clinical studies, the safety, efficacy and quality of a product. There can be no guarantee that the Corporation will succeed in obtaining regulatory approval from the FDA and the regulatory approvals of agencies in other countries to sell its products. All of the compounds of the Corporation, are still subject to clinical studies and if the results of such studies are not positive, the Corporation may not be in a position to make any filing to obtain the mandatory regulatory approval or it may have to perform additional clinical studies on any of its products until the results support the safety and efficacy of such product, therefore incurring additional delays and costs. The filing of a new drug application ("NDA") or biological license application ("BLA") is complex and the Corporation has never made any filings in order to obtain the regulatory approval of a product. Therefore, the Corporation shall rely in part on third-party suppliers to help it perform this task.

Furthermore, the obtaining of regulatory approval is subject to the discretion of regulatory agencies. Therefore, even if the Corporation has obtained positive results relating to the safety and efficacy of a product, a regulatory agency may not accept such results as being conclusive and allow the Corporation to sell its products in a given country. A regulatory agency may require that additional tests on the safety and efficacy of a product be conducted prior to granting approval, if any.

Even if the FDA approves a product, there can be no guarantee that other regulatory agencies will approve this product in their respective countries. Even if the Corporation obtains regulatory approval for any of its products, regulatory agencies have the power to limit the indicated use of a product as they see fit.

***The manufacture, marketing and sale of the products will be subject to ongoing and extensive governmental regulation in the country in which the Corporation intends to market its products.***

The manufacture, marketing and sale of the products will be subject to ongoing and extensive governmental regulation in the country in which the Corporation intends to market its products. For instance, if the Corporation obtains marketing approval for one product in the USA, the marketing of this product will be subject to extensive regulatory requirements administered by the FDA and other

regulatory bodies, such as adverse event reporting requirements in compliance with all of the FDA's marketing and promotional requirements. The manufacturing facilities for the Corporation's product will also be subject to continual review and periodic inspection and approval of manufacturing modifications. Manufacturing facilities are subject to inspections by the FDA and must comply with the FDA's GMP regulations. Failure to comply with any of these post-approval requirements can result in a series of sanctions, including withdrawal of the right to market a product. The failure to obtain or a delay in obtaining a FDA or other regulatory bodies' approval may postpone the Corporation's capacity to generate revenues and adversely materially affect its financial conditions and operating results.

***Clinical trials may not demonstrate a clinical benefit of the Corporation's product candidates.***

Clinical trials may not demonstrate a clinical benefit of the Corporation's product candidates. Positive results from pre-clinical studies and early clinical trials should not be relied upon as evidence that later stage or large scale clinical trials will succeed. The Corporation will be required to demonstrate with substantial evidence through well-controlled clinical trials that its product candidates are safe and effective for use in a diverse population before the Corporation can seek regulatory approvals for their commercial sale. Success in early clinical trials does not mean that future clinical trials will be successful because product candidates in later stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of regulatory authorities despite having progressed through initial clinical trials.

Even after the completion of phase 3 clinical trials, regulatory authorities may disagree with its clinical trial design and its interpretation of data, and may require the Corporation or its partners to conduct additional clinical trials to demonstrate the efficacy of its product candidates.

***The success of the Corporation's product candidates is influenced by its collaborations with its partners and any adverse developments in its relationship with its partners could materially harm its business.***

The success of the Corporation's product candidates is influenced by its collaborations with its partners. Any adverse developments in its relationship with its partners could materially harm its business. The Corporation is subject to a number of risks associated with any collaboration that could be entered into for the development of its product candidates, including the risk that these collaborators may terminate the relevant agreement(s) upon the occurrence of certain specified events, including a material breach by the Corporation of any of its obligations under the respective agreements.

***The Corporation's product candidates could cause undesirable and potentially serious side effects during clinical trials that could delay or prevent their regulatory approval or commercialization.***

The Corporation's product candidates could cause undesirable and potentially serious side effects during clinical trials that could delay or prevent their regulatory approval or commercialization. Undesirable side effects caused by any of its product candidates could cause the Corporation or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by regulatory authorities for any or all targeted indications. This, in turn, could prevent the Corporation from commercializing its product candidates and generating revenues from their sale. In addition, if its product candidates receive marketing approval and the Corporation or others later identify undesirable side effects caused by the product:

- regulatory authorities may withdraw their approval of the product;
- the Corporation may be required to recall the product, change the way the product is administered, conduct additional clinical trials or change the labelling of the product;
- a product may become less competitive and product sales may decrease; or
- Prometic's reputation may suffer.



Any one or a combination of these events could prevent the Corporation from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent the Corporation from generating revenues from the sale of the affected product.

***The FDA's (or equivalent body) review of new drugs based on safety, efficacy or other regulatory considerations may result in significant delays.***

The FDA's (or equivalent body) review of new drugs based on safety, efficacy or other regulatory considerations may result in significant delays in obtaining regulatory approvals, additional clinical trials being required, or more stringent product labelling requirements. Any delay in obtaining, or inability to obtain, applicable regulatory approvals may prevent the Corporation from commercializing our product candidates.

The Corporation's financial condition could be affected by the introduction of new regulations or amendments to existing regulations. New legislation or changes to existing legislation affecting the Corporation and its potential customers could decrease demand for the Corporation's products and affect its results of operation and financial condition. For example, the implementation of health care reform legislation that regulates drug costs could limit the profits that could be made from the development of new drugs. In addition, new laws or regulations could increase the Corporation's costs related to manufacturing therapeutics (for e.g. a change in source plasma specifications by the FDA could lead to more testing which could increase costs of source plasma, driving up costs of goods sold (COGs) for plasma-derived therapeutics).

***The Corporation may rely on third party suppliers of services to conduct its preclinical and clinical studies and the failure by such third parties to comply with their obligations may delay the studies and/or have an adverse effect on the Corporation's development program.***

The Corporation may rely on third party suppliers of services to conduct its preclinical and clinical studies and the failure by such third parties to comply with their obligations may delay the studies and/or have an adverse effect on the Corporation's development program. The Corporation has limited resources to conduct preclinical and clinical studies and may rely on third-party suppliers of services to conduct its studies. If the Corporation's third-party suppliers of services become unavailable for any reason, including as a result of the failure to comply with the rules and regulations governing the conduct of preclinical and clinical studies, operational failures, such as equipment failures or unplanned facility shutdowns, damage from any event, including fire, flood, earthquake, business restructuring or insolvency, or if they fail to perform their contractual obligations pursuant to the terms of the agreements entered into with the Corporation, such as failing to do the testing, compute the data or complete the reports further to the testing, the Corporation may incur delays in connection with the planned timing of its studies which could adversely affect the timing of the development program of a molecule and/or protein or delay the filing of an NDA or BLA. If the damage to any of the Corporation's third-party suppliers of services is extensive or if, for any reason, such suppliers do not operate in compliance with Good Clinical Practices or are unable or refuse to perform their contractual obligations, the Corporation will need to find alternative third-party suppliers of services.

If the Corporation is required to change or select new third-party suppliers of services, the timing of the work related to preclinical and/or clinical studies could be delayed since the number of competent and reliable third-party suppliers to conduct preclinical and clinical work in compliance with GLP is limited. Any selection of new third-party suppliers to carry out work related to preclinical and clinical studies will be time-consuming and will result in additional delays in receiving data, analysis and reports from such third-party suppliers which, in turn, will delay the obtaining of regulatory approval to commercialize the Corporation's products. Furthermore, such delays could increase the Corporation's expenditures to develop a product and materially adversely affect its operating results and financial condition.

***Failure to recruit and enrol patients for clinical trials may cause the development of the Corporation's product candidates to be delayed***

Failure to recruit and enrol patients for clinical trials may cause the development of the Corporation's product candidates to be delayed. The Corporation may encounter delays or rejections in recruiting enrolling enough patients to complete clinical trials. Patient enrolment depends on many factors, including the size of the patient population, the nature of the protocol, the proximity of patients to clinical sites, the number of suitable patients and the eligibility criteria for the clinical trial. Any delays in planned patient enrolment may result in delays to product development and increased development costs, which could harm its ability to develop products and materially adversely affect its operating results and financial condition.

***The Corporation does not know whether any of its ongoing or planned clinical trials will proceed or be completed on schedule, or at all.***

The Corporation does not know whether any of its ongoing or planned clinical trials will proceed or be completed on schedule, or at all. The commencement of its planned clinical trials could be substantially delayed or prevented by several factors, including:

- limited number of, and competition for, suitable patients with the indications required for enrolment in its clinical trials;
- limited number of, and competition for, suitable sites to conduct its clinical trials;
- delay or failure to obtain FDA or non-USA regulatory agencies' approval or agreement to commence a clinical trial;
- delay or failure to obtain sufficient supplies of the product candidate for its clinical trials;
- delay or failure to reach agreement on acceptable clinical trial agreement terms or clinical trial protocols with prospective sites or investigators; and
- delay or failure to obtain an institutional review board ("IRB") approval to conduct a clinical trial at a prospective site.

The completion of any clinical trial could also be substantially delayed or prevented by several factors, including:

- slower than expected rates of patient recruitment and enrolment;
- failure of patients to complete the clinical trial;
- unforeseen safety issues;
- lack of efficacy evidenced during any clinical trial;
- termination of any clinical trial by one or more clinical trial sites;
- inability or unwillingness of patients or medical investigators to follow a clinical trial protocols;
- inability to monitor patients adequately during or after treatment; and
- introduction of competitive products that may impede our ability to retain patients in any clinical trial.

Clinical trials may be suspended or terminated at any time by the FDA, other regulatory authorities, the IRB overseeing the clinical trial at issue, any of its clinical trial sites with respect to that site, or us. Any failure or significant delay in completing any clinical trial for its product candidates could materially harm its financial results and the commercial prospects for its product candidates.

***Governmental health administration authorities, private health coverage insurers and other organizations may not reimburse patients for the costs of the Corporation's, products and related treatment.***

Market acceptance of the Corporation's products is uncertain and depends on a variety of factors, some of which are not under the control of the Corporation. The Corporation's ability to commercialize its products with success will depend on a variety of factors. One of these is the extent to which reimbursement to patients for the cost of such products and related treatment will be made available by governmental health administration authorities, private health coverage insurers and other organizations. Obtaining reimbursement approval for a product is time-consuming and a costly process that could require the Corporation to provide supporting scientific, clinical and cost effectiveness data for the use of a product. There can be no guarantee the Corporation's data will be positive enough for third-party payers to accept to reimburse a Corporation product.

The Corporation has never made any application to seek reimbursement of a drug and must, therefore, rely in part on third-party suppliers of services to help it perform this task.

Other factors that will have an impact on the acceptance of the Corporation's products include:

- acceptance of the products by physicians and patients as safe and effective treatments;
- product price;
- the effectiveness of the Corporation's sales and marketing efforts (or those of its commercial partner);
- storage requirements and ease of administration;
- dosing regimen;
- safety and efficacy;
- prevalence and severity of side effects; and
- competitive products.

If government and third party payors fail to provide coverage and adequate reimbursement rates for the Corporation's product candidates, its revenues and potential for profitability will be reduced. The Corporation's product revenues will depend principally upon the reimbursement rates established by third party payors, including government health administration authorities, managed-care providers, public health insurers, private health insurers and other organizations. These third party payors are increasingly challenging the price, and examining the cost effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status, if any, of newly approved drugs, pharmaceutical products or product indications. We may need to conduct post-marketing clinical trials in order to demonstrate the cost-effectiveness of products. Such clinical trials may require us to dedicate a significant amount of management time and financial and other resources. If reimbursement of such product is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels, our revenues could be reduced. Moreover, the determination of the price of certain drugs in orphan disease indications could be even more difficult to make due to lack of comparables.

***The Corporation may rely in whole or in part on third parties for the manufacture and supply of its products and such reliance may adversely affect the Corporation if the third parties are unable to fulfill their obligations.***

The Corporation may rely in whole or in part on third parties for the manufacture and supply of its products and such reliance may adversely affect the Corporation if the third parties are unable to fulfill their obligations. The Corporation may not have the resources, facilities or experience to manufacture its products in large quantities on its own. The Corporation may rely on third parties to manufacture and supply products for clinical studies and, unless the Corporation deems the manufacture of this product

feasible and profitable if it is approved for commercialization, it may rely on third parties for some time to manufacture and supply large quantities of product for commercial sales. The Corporation's reliance on third-party manufacturers will expose it to a number of risks. If third-party manufacturers become unavailable to the Corporation for any reason, including as a result of the failure to comply with GMP regulations, manufacturing problems or other operational failures, such as equipment failures or unplanned facility shutdowns required to comply with GMP, damage from any event, including fire, flood, earthquake, business restructuring or insolvency, or if they fail to perform their contractual obligations under agreements with the Corporation, such as a failure to deliver the quantities requested on a timely basis, the Corporation may be delayed in manufacturing products and could be unable to meet the regulatory requirements of the FDA or other regulatory agencies to obtain market approval for its products. Any such event could delay the supply of a product to conduct clinical trials and, if a product has reached commercialization, could prevent the supply of the product and adversely affect the revenues of the Corporation. If the damage to a third-party manufacturer facility is extensive, or, for any reason, it does not operate in compliance with GMP or is unable or refuses to perform its obligations under its agreement with the Corporation, the Corporation will need to find an alternative third-party manufacturer. The selection of a third-party manufacturer will be time-consuming and costly since the Corporation will need to validate the manufacturing facility of such new third-party manufacturer. The validation will include an assessment of the capacity of such third-party manufacturer to produce the quantities that may be requested from time to time by the Corporation, the manufacturing process and its compliance with GMP. In addition, the third-party manufacturer will have to familiarize itself with the Corporation's technology. Any delay in finding an alternative third-party manufacturer of a product could result in a shortage of such product, delay clinical study programs and the filing for regulatory approval of a product, and deprive the Corporation of potential product revenues.

***The Corporation may build its own sales force or enter into a commercial agreement with a third party for the sale and marketing of its products and there is no guarantee that the Corporation will be able to achieve one of these tasks.***

The Corporation may build its own sales force or enter into a commercial agreement with a third party for the sale and marketing of its products and there is no guarantee that the Corporation will be able to achieve one of these tasks. The Corporation currently has limited marketing capabilities and a minimal sales force. In addition, the Corporation has limited experience in developing, training or managing a marketing or sales force. In order to commercialize its products, the Corporation must either develop its own sales force or enter into a commercial agreement with a third party. The development of a sales force is costly and will be time-consuming given the limited experience the Corporation has in that respect. To the extent the Corporation develops a sales force, the Corporation will be competing against companies who have more experience managing a sales force than the Corporation and access to more funds than the Corporation with which to manage a sales force. Consequently, there can be no guarantee that the sales force that the Corporation would develop would be efficient and would maximize the revenues derived from the sale of the Corporation's products.

Finding a third party for the sale and commercialization of a product is a lengthy process which includes the assessment of the services to be performed by the third party, a due diligence on the Corporation's products and the negotiation of the terms and conditions of a commercial agreement. The outcome of this process is uncertain and the Corporation may not be able to conclude a commercial agreement. If such an event occurs, the Corporation could have to delay the launch of its products which could adversely materially affect the financial conditions and the operating results of the Corporation.

***The failure by the Corporation to protect its intellectual property may have a material adverse effect on its ability to develop and commercialize its products.***

The failure by the Corporation to protect its intellectual property may have a material adverse effect on its ability to develop and commercialize its products. The Corporation will be able to protect its intellectual property rights from unauthorized use by third parties only to the extent that its intellectual property rights

are covered by valid and enforceable patents or are effectively maintained as trade secrets. The Corporation tries to protect its intellectual property license by filing patent applications related to its proprietary technology, inventions and improvements that are important to the development of its business. Because the patent position of pharmaceutical companies involves complex legal and factual questions, the issuance, scope and enforceability of patents cannot be predicted with certainty. Patents, if issued, may be challenged, invalidated or circumvented. If the Corporation's patents are invalidated or found to be unenforceable, it will lose the ability to exclude others from making, using or selling the inventions claimed. Moreover, an issued patent does not guarantee the Corporation the right to use the patented technology or commercialize a product using that technology. Third parties may have blocking patents that could be used to prevent the Corporation from developing its product candidates, selling its products or commercializing its patented technology. Thus, patents that the Corporation owns may not allow it to exploit the rights conferred by its intellectual property protection. Moreover, the Corporation's pending patent applications may not result in patents being issued. Even if issued, they may not be issued with claims sufficiently broad to protect its products and technologies or may not provide the Corporation with a competitive advantage against competitors with similar products or technologies. Furthermore, others may independently develop products or technologies similar to those that the Corporation has developed or discover the Corporation's trade secrets. In addition, the laws of many countries do not protect intellectual property rights to the same extent as the laws of Canada, Europe and the USA, and those countries may also lack adequate rules and procedures for defending intellectual property rights effectively. Although the Corporation has received many patents for its products, there can be no guarantee that the Corporation will receive patents in countries where it files patent applications for its products. As a result, the validity and enforceability of our patents cannot be predicted with certainty. In addition, the Corporation cannot guarantee that:

- the Corporation or Corporation's licensors were the first to make the inventions covered by each of our issued patents and pending patent applications;
- the Corporation or Corporation's licensors were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of the Corporation or Corporation's licensors' technologies;
- any of the Corporation or Corporation's licensors' pending patent applications will result in issued patents;
- any of the Corporation or Corporation's licensors' patents will be valid or enforceable;
- any patents issued to Prometic or Prometic's licensors and collaboration partners will provide the Corporation with any competitive advantages, or will not be challenged by third parties;
- the Corporation will develop or in-license additional proprietary technologies that are patentable; or
- the patents of others will not have an adverse effect on Prometic's business.

***The Corporation relies on trade secrets, know-how and technology, which are not protected by patents, to maintain its competitive position.***

The Corporation also relies on trade secrets, know-how and technology, which are not protected by patents, to maintain its competitive position. The Corporation tries to protect this information by entering into confidentiality undertakings with parties that have access to it, such as the Corporation's current and prospective suppliers, employees and consultants. Any of these parties may breach the undertakings and disclose the confidential information to the Corporation's competitors. Enforcing a claim that a third party illegally obtained and is using trade secrets is expensive and time consuming and the outcome is unpredictable. In addition, it could divert management's attention. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, the Corporation's competitive position could be harmed.

***The Corporation may not be able to protect its intellectual property rights throughout the world.***

The Corporation may not be able to protect its intellectual property rights throughout the world. Filing, prosecuting and defending patents on all of our product candidates and products, when and if the Corporation has any, in every jurisdiction would be prohibitively expensive. Competitors may use our technologies in jurisdictions where the Corporation or its licensors have not obtained patent protection to develop our own products. These products may compete with our products, when and if the Corporation has any, and may not be covered by any of its or its licensors' patent claims or other intellectual property rights.

***The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of Canada and USA, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions.***

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of Canada and USA, and many companies have encountered significant problems in protecting and defending such rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favour the enforcement of patents and other intellectual property protection, particularly those relating to biotechnology and/or pharmaceuticals, which could make it difficult for the Corporation to stop the infringement of our patents. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

***Patent protection for the Corporation's product candidates or products may expire before it is able to maximize their commercial value which may subject the Corporation to increased competition and reduce or eliminate its opportunity to generate product revenue.***

Patent protection for the Corporation's product candidates or products may expire before it is able to maximize their commercial value which may subject the Corporation to increased competition and reduce or eliminate its opportunity to generate product revenue. The patents for its product candidates have varying expiration dates and, when these patents expire, the Corporation may be subject to increased competition and may not be able to recover its development costs. In some of the larger economic territories, such as Canada, the USA and Europe, patent term extension/restoration may be available to compensate for time taken during aspects of the product candidate's regulatory review. However, the Corporation cannot be certain that an extension will be granted, or if granted, what the applicable time period or the scope of patent protection afforded during any extended period will be. In addition, even though some regulatory agencies may provide some other form of exclusivity for a product candidate under its own laws and regulations, the Corporation may not be able to qualify the product candidate or obtain the exclusive time period.

If the Corporation is unable to obtain patent term extension/restoration or some other exclusivity, the Corporation could be subject to increased competition and its opportunity to establish or maintain product revenue could be substantially reduced or eliminated. Furthermore, the Corporation may not have sufficient time to recover its development costs prior to the expiration of its Canadian and non-Canadian patents.

***The Corporation may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights and may be unable to protect its rights to, or use of, its technology.***

The Corporation may incur substantial costs as a result of litigation or other proceedings relating to patent and other intellectual property rights and may be unable to protect its rights to, or use of, its technology. If the Corporation chooses to go to court to restrain a third party from using the inventions claimed in its patents or licensed patents, that individual or corporation has the right to ask the court to rule that these patents are invalid and/or should not be enforced against that third party. These lawsuits are expensive

and would consume time and other resources even if the Corporation was successful in stopping the infringement of these patents. In addition, there is a risk that the court will decide that these patents are invalid or unenforceable and that the Corporation does not have the right to retrain the third party from using the inventions. There is also the risk that, even if the validity of these patents is upheld, the court will refuse to grant a decision or judgment in the Corporation's favour on the ground that such other party's activities do not infringe the Corporation's rights.

If the Corporation wishes to use the technology or compound claimed in issued and unexpired patents owned by a third party, the Corporation will need to obtain a license from such third party, enter into litigation to challenge the validity or enforceability of the patents or incur the risk of litigation in the event that the owner asserts that the Corporation infringed its patents. The failure to obtain a license to technology or the failure to challenge an issued patent that the Corporation may require to develop or commercialize its product candidates may have a material adverse impact on the Corporation's operating results and financial condition.

If a third party asserts that the Corporation infringed their patents or other proprietary rights, the Corporation could face a number of risks that could seriously harm its results of operations, financial condition and competitive position, including:

- patent infringement and other intellectual property claims, which would be costly and time consuming to defend, whether or not the claims have merit, and which could delay the regulatory approval process and divert management's attention from our business;
- substantial damages for past infringement, which the Corporation may have to pay if a court determines that its product candidates or technologies infringe a competitor's patent or other proprietary rights;
- a court prohibiting the Corporation from selling or licensing its technologies or future drugs unless the third party licenses its patents or other proprietary rights to the Corporation on commercially reasonable terms, which it is not required to do; and
- if a license is available from a third party, the Corporation may have to pay substantial royalties or lump sum payments or grant cross licenses to its patents or other proprietary rights to obtain that license.

The biopharma industry has produced a proliferation of patents, and it is not always clear to industry participants, including the Corporation, which patents cover various types of products or methods of use. The coverage of patents is subject to interpretation by the courts, and the interpretation is not always uniform. If the Corporation is sued for patent infringement, the Corporation would need to demonstrate that its product candidates or methods of use either do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid, and the Corporation may not be able to do this. Proving invalidity, in particular, is difficult since it requires a showing of clear and convincing evidence to overcome the presumption of validity enjoyed by issued patents.

Canadian patent laws as well as the laws of some foreign jurisdictions provide for provisional rights in published patent applications beginning on the date of publication, including the right to obtain reasonable royalties, if a patent is subsequently issued and certain other conditions are met. While the Corporation believes that there may be multiple grounds on which to challenge the validity of the Canadian patent and the foreign counterparts, the Corporation cannot predict the outcome of any invalidity challenge. Alternatively, it is possible that the Corporation may determine it prudent to seek a license from the patent holder to avoid potential litigation and other potential disputes. The Corporation cannot be sure that a license would be available to the Corporation on acceptable terms, or at all.

Because some patent applications in the USA may be maintained in secrecy until the patents are issued, because patent applications in Canada and many foreign jurisdictions are typically not published until 18 months after filing, and because publications in the scientific literature often lag behind actual discoveries,

the Corporation cannot be certain that others have not filed patent applications for technology covered by its licensors' issued patents or its pending applications or its licensors' pending applications, or that the Corporation or its licensors were the first to invent the technology.

Patent applications filed by third parties that cover technology similar to the Corporation's may have priority over its or its licensors' patent applications and could further require the Corporation to obtain rights to issued patents covering such technologies. If another party files a USA patent application on an invention similar to the Corporation's, the Corporation may elect to participate in or be drawn into an interference proceeding declared by the USA Patent and Trademark Office (USPTO) to determine priority of invention in the USA. The costs of these proceedings could be substantial, and it is possible that such efforts would be unsuccessful, resulting in a loss of our USA patent position with respect to such inventions.

Some of its competitors may be able to sustain the costs of complex patent litigation more effectively than the Corporation can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on its ability to raise the funds necessary to continue its operations. The Corporation cannot predict whether third parties will assert these claims against the Corporation or against its licensors, or whether those claims will harm our business. If the Corporation is forced to defend against these claims, whether they are with or without any merit, whether they are resolved in favour of or against the Corporation or its licensors, the Corporation may face costly litigation and diversion of management's attention and resources. As a result of these disputes, the Corporation may have to develop costly non-infringing technology, or enter into licensing agreements. These agreements, if necessary, may be unavailable on terms acceptable to the Corporation, if at all, which could seriously harm its business or financial condition.

The Corporation's commercial success depends, in part, on its ability not to infringe on third parties' patents and other intellectual property rights. The Corporation's capacity to commercialize its products will depend, in part, on the non-infringement of third parties' patents and other intellectual property rights. The biopharmaceutical and pharmaceutical industries have produced a multitude of patents and it is not always clear to participants, including the Corporation, which patents cover various types of products or methods of use. The scope and breadth of patents is subject to interpretation by the courts and such interpretation may vary depending on the jurisdiction where the claim is filed and the court where such claim is litigated. The holding of patents by the Corporation for its products and their applications does not guarantee that the Corporation is not infringing on other third parties' patents and there can be no guarantee that the Corporation will not be in violation of third parties' patents and other intellectual property rights. Patent analysis for non-infringement is based in part on a review of publicly available databases. Although the Corporation reviews from time to time certain databases to conduct patent searches, it does not have access to all databases. It is also possible that some of the information contained in the databases has not been reviewed by the Corporation or was found to be irrelevant at the time the searches were conducted. In addition, because patents take years to be issued, there may be currently pending applications that the Corporation is unaware of which may later be issued. As a result of the foregoing, there can be no guarantee that the Corporation will not violate third-party patents. Because of the difficulty in analyzing and interpreting patents, there can be no guarantee that a third party will not assert that the Corporation infringes upon any of its patents or any of its other intellectual property rights.

There is no guarantee that the Corporation will not become involved in litigation. Litigation with any third party, even if the allegations are without merit, is expensive, time-consuming and will divert management's attention from the daily execution of the Corporation's business plan. Litigation implies that a portion of the Corporation's financial assets would be used to sustain the costs of litigation instead of being allocated to further the development of its business plan. If the Corporation is involved in patent infringement litigation, it will need to demonstrate that its products do not infringe the patent claims of the relevant patent, that the patent claims are invalid or that the patent is unenforceable. If the Corporation



was found liable for infringement of third parties' patents or other intellectual property rights, the Corporation could be required to enter into royalty or licensing agreements on terms and conditions that may not be favourable to the Corporation, and/or pay damages, including up to treble damages (but only if found liable of willful infringement) and/or cease the development and commercialization of its products. Any finding that the Corporation is guilty of patent infringement could materially adversely affect the business, financial conditions and operating results of the Corporation.

The Corporation has not been served with any notice that it is infringing on a third party patent, but there may be issued patents that the Corporation is unaware of that its products may infringe, or patents that the Corporation believes it does not infringe but could be found to be infringing.

***The Corporation faces competition and the development of new products by other companies could materially adversely affect the Corporation's business and its products.***

The Corporation faces competition and the development of new products by other companies could materially adversely affect the Corporation's business and its products. The biopharmaceutical and pharmaceutical industries are highly competitive and the Corporation must compete with pharmaceutical companies, biotechnology companies, academic and research institutions as well as governmental agencies for the development and commercialization of products. Some of these competitors develop products in the indications in which the Corporation is involved and could be considered direct or indirect competitors.

In the other indications currently being studied by the Corporation for development, there may exist companies that are at a more advanced stage of developing a product to treat those same diseases. Some of these competitors have capital resources, research and development personnel and facilities that are superior to the Corporation's. In addition, some competitors are more experienced than the Corporation in the commercialization of medical products and already have a sales force in place to launch new products. Consequently, they may be able to develop alternative forms of medical treatment which could compete with the products of the Corporation and commercialize them more rapidly and effectively than the Corporation.

***The Corporation depends on its key personnel to research, develop and bring new products to the market and the loss of key personnel or the inability to attract highly qualified individuals could have a material adverse effect on its business and growth potential.***

The Corporation depends on its key personnel to research, develop and bring new products to the market and the loss of key personnel or the inability to attract highly qualified individuals could have a material adverse effect on its business and growth potential. The Corporation's mission is to discover or acquire novel therapeutic products targeting unmet medical needs in attractive specialty markets. The achievement of this mission requires qualified scientific and management personnel. The loss of scientific personnel or of members of management could have a material adverse effect on the business of the Corporation. In addition, the Corporation's growth is and will continue to be dependent, in part, on its ability to retain and hire qualified scientific personnel. There can be no guarantee that the Corporation will be able to continue to retain its current employees or will be able to attract qualified personnel to pursue its business plan.

***The Corporation depends on its founder and current President and CEO, Mr. Pierre Laurin, in the short and long-term to bring the Corporation's corporate and business plan to execution.***

The Corporation depends on its founder and current President and CEO, Mr. Pierre Laurin, in the short and long-term to bring the Corporation's corporate and business plan to execution. The loss of Mr. Laurin and the inability to identify internally or attract externally an appropriately highly qualified individual to replace him could have a material adverse effect on the Corporation's business and growth potential. The achievement of the Corporation's corporate and business plan requires a CEO, who is well versed in various scientific fields and related specialty markets as well as in raising funds privately or publicly. The

loss or departure of Mr. Laurin, Prometic's current President and CEO and founder of Prometic, who has built excellent personal relationships with both corporate and business strategic partners as well as Prometic's investors, could have a material adverse effect on the business of the Corporation. In addition, the Corporation's growth is and will continue to be dependent, in part, on his abilities to lead management in various fields and jurisdictions and raise funds. There can be no guarantee that the Corporation will be able to continue to retain its current President and CEO or will be able to identify internally or attract externally an appropriately highly qualified individual to replace him to pursue its corporate and business plan.

***The Corporation is not profitable and may never achieve profitability.***

The Corporation is not profitable and may never achieve profitability. The Corporation has been reporting losses since its inception. The Corporation will need to generate significant revenues to achieve profitability. There is no guarantee that the Corporation will succeed in commercializing its products, controlling its expenses and developing additional products, and, therefore, it may never become profitable.

***The Corporation may require additional funding and may not be able to raise the capital necessary to continue and complete the R&D of its products and their commercialization.***

The Corporation may require additional funding and may not be able to raise the capital necessary to continue and complete the R&D of its products and their commercialization. The Corporation generates revenues but is not profitable and needs financing in order to continue its activities. In the past, the Corporation has been financed through debt and public equity offerings and the Corporation may effect additional equity offerings to raise capital, the size of which cannot be predicted. The issuance and sales of substantial amounts of equity or other securities, or the perception that such issuances and sales may occur, could adversely affect the market price of the Common Shares.

***The market conditions or the business performance of the Corporation may prevent it from having access to the public markets in the future.***

The market conditions or the business performance of the Corporation may prevent it from having access to the public markets in the future. Therefore, there can be no guarantee that the Corporation will be able to continue to raise capital by way of public equity offerings. In such a case, the Corporation will have to use other means of financing, such as issuing debt instruments or entering into private financing agreements, the terms and conditions of which may not be favourable to the Corporation. These debt instruments may contain terms and conditions (e.g. covenants, etc.) which may be challenging or difficult for the Corporation to respect, may be breached or trigger default provisions. Accordingly, the Corporation may be required to compensate counterparties, for costs and losses incurred as a result of various events, including breaches of representations and warranties, covenants, claims that may arise during the terms of said debt instruments or as a result of litigation that may be suffered by counterparties. If adequate funding is not available to the Corporation, it may be required to delay, reduce or eliminate its R&D of new products, its clinical trials or its marketing and commercialization efforts to launch and distribute new products.

***The Corporation may not achieve its publicly-announced milestones in due time.***

The Corporation may not achieve its publicly-announced milestones in due time. From time to time, the Corporation publicly announces the timing of the occurrence of certain events. These statements are forward-looking and are based on management's best estimate relating to the occurrence of such events. However, the actual timing of such events may differ from what has been publicly disclosed. These variations may occur as a result of a series of events, including the nature of the results obtained during a clinical trial or during a research phase, problems with a supplier or any other event having the effect of delaying the timeline publicly announced. The Corporation's policy on forward-looking information does not consist in updating such information if the publicly disclosed timeline varies, unless otherwise required

to do so by law. Any variation in the timing of certain events having the effect of postponing such events could have an adverse material effect on the business plan, financial conditions or operating results of the Corporation.

***The development and commercialization of drugs could expose the Corporation to liability claims which could exceed its insurance coverage.***

The development and commercialization of drugs could expose the Corporation to liability claims which could exceed its insurance coverage. A risk of product liability claims is inherent in the development and commercialization of human therapeutic products. Product liability insurance is very expensive and offers limited protection. A product liability claim against the Corporation could potentially be greater than the coverage offered and, therefore, have a material adverse effect upon the Corporation and its financial position. Furthermore, a product liability claim could tarnish the Corporation's reputation, whether or not such claims are covered by insurance or are with or without merit.

***The Corporation may not receive the full payment of all milestones or royalty payments pursuant to the agreements entered into with third parties.***

The Corporation may not receive the full payment of all milestones or royalty payments pursuant to the agreements entered into with third parties and, consequently, the financial conditions and the operating results of the Corporation could be adversely impacted. The Corporation has entered into license agreements and other forms of agreements with third parties regarding the development and commercialization of some of its technologies and products. These agreements generally require that the third party pays to the Corporation certain amounts upon the attainment of various milestones and possibly include royalties on the sale of the developed product. There can be no guarantee that the Corporation will receive the payments described in those agreements since the development of the products may be cancelled if the research does not yield positive results. Under such circumstances, the Corporation would not receive royalties as well. Even if the development of a product yields positive results, all of the risks described herein with respect to the obtaining of regulatory approval are applicable. Finally, if there occurs a disagreement between the Corporation and the third party, the payment relating to the attainment of milestones or of royalties may be delayed. The occurrence of any of those circumstances could have a material adverse effect on the Corporation's financial condition and operating results.

***If the Corporation breaches any of the agreements under which it licenses rights to its product candidates or technology from third parties, it could lose license rights that are important to its business.***

If the Corporation breaches any of the agreements under which it licenses rights to its product candidates or technology from third parties, it could lose license rights that are important to its business. The Corporation licenses the development and commercialization rights for certain product candidates, and could, potentially, enter into similar licenses for other products in the future. Under these licenses, the Corporation is subject to various obligations, including royalty and milestone payments, annual maintenance fees, limits on sublicensing, insurance obligations and the obligation to use commercially reasonable best efforts to develop and exploit the licensed technology. If the Corporation fails to comply with any of these obligations or otherwise breach these agreements, its licensors may have the right to terminate the license in whole or in part or to terminate the exclusive nature of the license. Loss of any of these licenses or the exclusivity rights provided therein could harm its financial condition and operating results.

***The Corporation may be subject to damages resulting from claims that the Corporation, or its employees or consultants, have wrongfully used or disclosed alleged trade secrets of third parties.***

The Corporation may be subject to damages resulting from claims that the Corporation, or its employees or consultants, have wrongfully used or disclosed alleged trade secrets of third parties. Many of its employees were previously employed, and certain of its consultants are currently employed, at universities, public institutions, biotechnology or pharmaceutical companies, including its competitors or potential competitors. Although the Corporation has not received any claim to date, the Corporation may be subject to claims that the Corporation, or these employees or consultants, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of these current or former employers. Litigation may be necessary to defend against these claims.

If the Corporation fails in defending such claims, in addition to paying monetary damages, the Corporation may lose valuable intellectual property rights or personnel. The Corporation may be subject to claims that employees of its partners or licensors of technology licensed by the Corporation have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. The Corporation may become involved in litigation to defend against these claims. If the Corporation fails in defending such claims, in addition to paying monetary damages, the Corporation may lose valuable intellectual property rights or personnel.

***Disruptions to information technology systems of the Corporation could materially adversely affect the Corporation's business.***

Disruptions to information technology systems of the Corporation could materially adversely affect the Corporation's business. The Corporation depends on its information technology systems for the efficient functioning of its business, including financial reporting, accounting and data storage.

Management believes that the Corporation's information technology architecture is resilient, relying on redundant material components to prevent material failures, redundant telecommunication links to prevent communication failures. However, systems may be subject to damage or interruption resulting from power outages, telecommunication failures, computer viruses, security breaches, cyber-attacks and catastrophic events. Difficulties with the hardware and software platform may require the Corporation to incur substantial costs to repair or replace it, could result in a loss of critical data and could disrupt operations, which could have a material adverse effect on the Corporation's business and financial results. Prolonged disruptions to information technology systems may reduce the efficiency of the Corporation's entire operation, which could materially adversely affect its business.

***Data Security Incidents and Privacy Breaches could result in important remediation costs, increased cyber security costs, lost revenues and litigation and reputational harm.***

Data Security Incidents and Privacy Breaches could result in important remediation costs, increased cyber security costs, lost revenues and litigation and reputational harm. Cyber incidents can result from deliberate attacks or unintentional events. Cyber-attacks and security breaches could include unauthorized attempts to access, disable, improperly modify or degrade the Corporation's information, systems and networks, the introduction of computer viruses and other malicious codes and fraudulent "phishing" e-mails that seek to misappropriate data and information or install malware onto users' computers. Cyber-threats in particular vary in technique and sources, are persistent, frequently change and increasingly more targeted and difficult to detect and prevent against. Cyber-attacks could also result in important remediation costs, increased cyber security costs, lost revenues due to a disruption of activities, litigation and reputational harm affecting customer and investor confidence, which could materially adversely affect the Corporation's business and financial results.

***The Corporation may be subject to environmental remediation obligations or other obligations under environmental laws and regulations and climate change could exacerbate certain of the threats facing the Corporation's business.***

The Corporation may be subject to environmental remediation obligations or other obligations under environmental laws and regulations and climate change could exacerbate certain of the threats facing the Corporation's business. The Corporation is subject to laws and regulations concerning the environment, safety matters, regulation of chemicals and product safety in the countries where it operates its business. These requirements include regulation of the handling, manufacture, transportation, use and disposal of materials, including the discharge of pollutants into the environment. In the normal course of the Corporation's business, hazardous substances may be released into the environment, which could cause environmental or property damage or personal injuries, and which could subject the Corporation to remediation obligations regarding contaminated soil and groundwater or potential liability for damage claims.

In addition, global climate change could exacerbate certain of the threats facing the Corporation's business, including the business continuity depends on how well the Corporation protects its facilities and equipment. Several areas of the Corporation's operations further raise environmental considerations, such as greenhouse gas emissions and disposal of hazardous residual materials. Failure to recognize and adequately respond to changing governmental and public expectations on environmental matters could result in fines, missed opportunities, additional regulatory scrutiny or harm to the Corporation's brand and reputation which could potentially have an advance effect on the Corporation's business and financial results.

***The Corporation's Common Share price is volatile and investors could lose money as a result of such volatility.***

The Corporation's Common Share price is volatile and investors could lose money as a result of such volatility. General market conditions as well as differences between the Corporation's financial, scientific and clinical results and the expectations of investors as well as securities analysts can have a significant impact on the trading price of the Common Shares. In recent years, the shares of many biopharmaceutical companies have experienced extreme price fluctuations, unrelated to the operating performance of the affected companies. There can be no assurance that the market price of the Common Shares will not continue to experience significant fluctuations in the future, including fluctuations that are unrelated to the Corporation's performance. The occurrence of any of the above risks and uncertainties could have a material adverse effect on the price of the Common Shares.

## **8. DIVIDENDS**

To date, and despite not having any restriction preventing it from doing so, the Corporation has not paid any dividends in respect of any class of shares in its share capital, and it does not anticipate paying dividends in the short term. At the present time, the practice of the board of directors of the Corporation is to reinvest all available funds in operating activities.

## **9. DESCRIPTION OF CAPITAL STRUCTURE**

The Corporation is authorized to issue an unlimited number of Common Shares, and an unlimited number of preferred shares issuable (the "**Preferred Shares**") in series. As of March 23, 2017, 668,691,694 Common Shares were issued and outstanding and no Preferred Shares were issued.

### **9.1. Common Shares**

The holders of Common Shares are entitled to one vote per share at all meetings of the shareholders, and are entitled to receive dividends, as may be declared from time to time by the Board of Directors. In

the event of the voluntary (or involuntary) liquidation, dissolution, winding up or other distribution of the assets of the Corporation, the holders of Common Shares are entitled to receive the remaining property of the Corporation, subject to the preference rights of the holders of Preferred Shares, if any.

#### *Take-Over Bid Protection*

At the Corporation's annual meeting of its shareholders held on May 3, 2006, two shareholders rights plans were adopted, and came into force. Both shareholders rights plans were re-adopted at Prometic's annual meetings of shareholders held on May 6, 2009, May 9, 2012, and May 13, 2015.

The rights issued under the first plan will become exercisable only if a person or entity acquires or announces an intention to acquire shares for a total ownership of 20% or more of the Corporation's outstanding Common Shares in an unsolicited takeover bid, unless such acquisition meets certain requirements intended to protect the interests of all shareholders in a "permitted bid". Each such right will entitle its holder to purchase Common Shares of the Corporation at a substantial discount to the market value of such shares at the time of exercise. A "permitted bid" is one made to all shareholders by way of a takeover bid circular prepared in accordance with applicable securities laws, which remains open for a minimum of 60 days, and is accepted by the holders of not less than 50% of the shares held by shareholders other than the proposed acquiror and its related parties, among other conditions. In certain cases, the bid must be extended to allow more time for shareholders to tender.

The second shareholder rights plan seeks to maximize shareholder value by spinning-off the Corporation's subsidiaries, PBI and PBP, to the benefit of all shareholders in the event of an unsolicited takeover bid. Therapeutics in development by this subsidiary could have a high potential value and, for that reason, could induce an interested party to make a hostile takeover bid on Prometic. This spin-off shareholder rights plan reduces the incentive for an offeror to avail itself of a low market capitalization of the Corporation through a take-over bid, instead of negotiating a commercial transaction that reflects the full value for PBI's or PBP's rights and other assets. Rights issued under this second shareholder rights plan will become exercisable in the event of an unsolicited offer and will entitle their holders to purchase Class A shares of PBI and Class A shares of PBP at an exercise price of \$0.00001 per subsidiary share, the whole subject to compliance with securities laws.

Rights under each shareholder rights plan were issued to all shareholders. They are automatically attached to all Common Shares of the Corporation already issued and outstanding on the date the plans came into force. Rights will also be issued thereafter upon any future issuance of Common Shares of the Corporation prior to Separation Time (as defined under each plan). Under each plan, the bidder or bidders and persons acting in concert with them will not be entitled to exercise such rights and the Corporation may redeem all rights at any time prior to a takeover.

## **9.2. Preferred Shares**

The directors of the Corporation may issue Preferred Shares in one or more series, each series to consist of such number of shares as determined by the directors, which may also fix the designation, rights, restrictions, conditions and limitations to be attached to the Preferred Shares of each series.

The holders of Preferred Shares, if any, do not have any voting rights for the election of directors or for any other purpose, nor are they entitled to attend meetings of the shareholders, except as to any amendment to the rights, privileges, restrictions and conditions attached to the Preferred Shares, which amendment must be approved by at least 2/3 of the votes cast at a meeting of the holders of Preferred Shares called for that purpose.

The holders of Preferred Shares are entitled to dividends, and have preference over the other classes of shares (including Common Shares) with respect to payment of dividends.

In the event of liquidation, dissolution or winding up of the Corporation or other distribution of the assets of the Corporation, the holders of Preferred Shares are entitled to receive in preference to the holders of any other classes of shares: (i) an amount equal to the amount paid up on such shares, together with, in the case of cumulative dividends, all unpaid cumulative dividends and, in the case of non-cumulative dividends, all declared and unpaid non-cumulative dividends, and (ii) if the liquidation, dissolution, winding-up or distribution is voluntary, an additional amount equal to the premium, if any, that would have been payable on the redemption of the Preferred Shares.

The Preferred Shares are redeemable or may be purchased for cancellation by the Corporation at such times and at such prices and upon such conditions as may be specified in the rights, privileges, restrictions and conditions attached to the relevant series.

## 10. MARKET FOR SECURITIES

### 10.1. Trading Price and Volume

The Common Shares are listed on the TSX under the symbol “PLI”. The table below indicates the price ranges on a per share basis and the volume traded on a monthly basis during the 2016 Financial Year.

Month	High Price	Low Price	Close Price	Trading Volume
January 2016	\$3.59	\$2.33	\$2.53	48,900,577
February 2016	\$2.79	\$1.88	\$2.61	33,700,465
March 2016	\$3.49	\$2.65	\$3.08	52,139,894
April 2016	\$3.49	\$3.04	\$3.27	23,787,153
May 2016	\$3.35	\$2.80	\$2.80	29,517,446
June 2016	\$3.11	\$2.67	\$2.79	27,773,122
July 2016	\$3.14	\$2.71	\$3.07	15,688,854
August 2016	\$3.15	\$2.66	\$2.79	22,708,408
September 2016	\$3.06	\$2.77	\$2.92	19,945,243
October 2016	\$3.24	\$2.77	\$2.82	29,174,613
November 2016	\$2.92	\$2.05	\$2.43	58,729,691
December 2016	\$2.44	\$1.47	\$2.23	86,982,606

## 11. ESCROWED SECURITIES

As of March 23, 2017, to the knowledge of the Corporation, the following number of securities of the class identified below, are held in escrow:

Escrowed Securities		
Designation of Class	Number of Securities held in Escrow	Percentage of Class
Common Shares	450,000	0.07%

450,000 shares were placed in escrow with Computershare Trust Company of Canada, as escrow agent, by Mr. Pierre Laurin, President and Chief Executive Officer of the Corporation, as security for a loan by the Corporation in the amount of \$450,000 granted in order to enable Mr. Laurin to exercise options to acquire Common Shares. Mr. Laurin repaid \$105,133 which was applied against accumulated interest, making the amount owed as of March 23, 2017 equal to \$400,000. The loan was last amended on February 25, 2016. The February 25, 2016 amendment provides for the loan to bear interest at a rate equal to the Bank of Canada's prime rate plus 1% per annum and stipulates that the loan is repayable upon the earlier of (i) March 31, 2019 or (ii) thirty (30) days preceding a targeted NASDAQ or NYSE listing date of the Common Shares.

## 12. DIRECTORS AND EXECUTIVE OFFICERS

### 12.1. Directors and Executive Officers

The two following tables set out the names, province or state of residence of the directors and officers of the Corporation as of March 23, 2017, their positions with the Corporation, their present principal occupation and, when they are directors of the Corporation, the year in which they were appointed. The present term of each director will expire immediately prior to the next annual meeting of the shareholders of the Corporation.

#### Directors

Directors			
Name and Province or State and Country of Residence	Board and Committees Membership	Director Since	Current Principal Occupation
<b>Pierre Laurin</b> Québec, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ PSDAM Committee<sup>(1)</sup></li> </ul>	1994	President and Chief Executive Officer of the Corporation
<b>Simon Best</b> Edinburgh, UK	<ul style="list-style-type: none"> <li>○ Chairman of the Board</li> <li>○ Audit &amp; Risk Committee</li> <li>○ HR and Compensation Committee</li> <li>○ Corporate Governance and Nominating Committee</li> <li>○ Defense Strategy Committee (Chair)</li> <li>○ PSDAM Committee (Chair)</li> </ul>	2014	Chairman of Sunergos Innovations Ltd. since September 2015
<b>Andrew Bishop</b> Ontario, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ Audit &amp; Risk Committee</li> <li>○ Defense Strategy Committee</li> </ul>	2015	Co-Founder/Partner of Bingley Capital Inc. since 2009



## Directors

Name and Province or State and Country of Residence	Board and Committees Membership	Director Since	Current Principal Occupation
<b>Stefan Clulow</b> Ontario, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ PSDAM Committee</li> </ul>	2014	Managing Director and Chief Investment Officer of Thomvest Asset Management Inc. and Managing Director of Thomvest Seed Capital Inc. since May 2010
<b>Kenneth Galbraith</b> British Columbia, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ HR and Compensation Committee</li> <li>○ PSDAM Committee</li> </ul>	August 10, 2016	Mr. Ken Galbraith is Managing Director of Five Corners Capital since 2013
<b>Raymond Hakim<sup>(2)</sup></b> Tennessee, USA	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ HR and Compensation Committee</li> <li>○ Corporate Governance and Nominating Committee</li> </ul>	2013	Clinical Professor of Medicine at Vanderbilt University Medical Center since January 2011
<b>Charles Kenworthy</b> California, USA	<ul style="list-style-type: none"> <li>○ Board</li> </ul>	2013	Executive Vice-President of Abraxis BioScience, LLC since 2011
<b>Louise Ménard</b> Québec, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ HR and Compensation Committee</li> <li>○ Corporate Governance and Nominating Committee</li> <li>○ Defense Strategy Committee</li> </ul>	2009	President, Groupe Méfor inc. since 1997
<b>Paul Mesburis</b> Ontario, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ Audit &amp; Risk Committee</li> <li>○ Corporate Governance and Nominating Committee</li> <li>○ Defense Strategy Committee</li> </ul>	2009	Managing Principal, Empryean Capital
<b>John Moran</b> California, USA	<ul style="list-style-type: none"> <li>○ Board</li> </ul>	2012	Chief Medical Officer of the Corporation
<b>Nancy Orr</b> Québec, Canada	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ Audit &amp; Risk Committee</li> <li>○ HR and Compensation Committee</li> <li>○ Defense Strategy Committee</li> </ul>	2010	Consultant
<b>Bruce Wendel</b> Connecticut, USA	<ul style="list-style-type: none"> <li>○ Board</li> <li>○ PSDAM Committee</li> </ul>	2008	Chief Strategy Officer of Hepalink USA since June 2012

(1) Plasma Strategy Development and Asset Monetization Committee

(2) Dr. Raymond Hakim will not stand for re-election at the next Annual General and Special Meeting of Shareholders to be held on May 10, 2017

## **Biographies**

The following are brief profiles of the executive officers and directors of the Corporation, including a description of each individual's principal occupation within the past five years.

### *Non-Executives Directors*

**Simon Geoffrey Best, Chairman of the Board.** Prof. Best is a seasoned veteran of the global Lifescience Industry with experience, both as a Founder, Chief Executive Officer and Chairman or Board Member of entrepreneurial companies and as a Chairman or Board Member of major industry bodies and public sector institutions, in the UK, USA, Europe, Asia and Latin America including the UK BioIndustry Association (BIA) and the US Biotechnology Industry Organization (BIO). He is also an experienced Angel, Venture Capital and Private Equity investor. In 1999, the World Economic Forum nominated him a Global Leader of Tomorrow and in 2000, a Technology Pioneer of the Year. In 1999, he was nominated as "Science and Technology Venturer of the Year" by the Financial Times. He was awarded the London Business School Alumni Achievement Prize in 2007. He holds an MBA from London Business School and an Honorary Doctorate and B.Mus from York University. In 2007, he was elected a Fellow of the Royal Society of Edinburgh. In 2008, he was awarded an OBE by Queen Elizabeth II and appointed a Visiting Professor of Medicine by the University of Edinburgh. On November 4, 2015, Prof. Best was elected to the board of directors of Evofem Inc., a women's health company based in San Diego. From March 2010 to August 2015, Prof. Best was the Chairman of Edinburgh BioQuarter with responsibility for company formation and technology transfer for the University of Edinburgh. In September 2015, this entity was replaced by Sunergos Innovations Limited. Sunergos was reabsorbed by the University in February 2017 after which Prof. Best continued to serve as a Senior Advisor. Prof. Best held also the position of Chief Executive Officer at Aquapharm Biodiscovery Ltd. (a company in the sector of drug discovery) from May 2010 to November 2012.

**Andrew Bishop.** Mr. Bishop is a Partner and Co-Founder of Bingley Capital Inc., and brings over 20 years of experience in advising biotech and health care companies. He has worked on over 100 financing and M&A transactions over his career. Prior to establishing Bingley Capital in 2009, he held senior roles in investment banking, including Head of Health Care Investment Banking at HSBC Securities (Canada) Inc., where he covered biotech, pharma, and specialty pharma companies. He started his career in investment banking focused on companies in Quebec. For the past 9 years, Mr. Bishop served as a Director and Chair of Willow Breast & Hereditary Cancer Support, a not-for-profit organization focused on breast and hereditary cancer. Mr. Bishop received an International M.B.A. (with Distinction) from the Schulich School of Business at York University, and a Bachelor of Arts in Political Science and Economics from McGill University. He also received his Chartered Financial Analyst designation.

**Stefan Clulow.** Mr. Stefan Clulow is Managing Director and Chief Investment Officer of Thomvest Asset Management Inc. since July 2014 and Managing Director of Thomvest Seed Capital Inc. since May 2010. Prior to joining Thomvest, Stefan practiced law in Silicon Valley, California and Toronto, Ontario. Mr. Clulow sits on the boards of a number of private companies and charitable organizations. Mr. Clulow received a B.A. and an LL.B. from McGill University. He is a member of the State Bar of California and the Law Society of Upper Canada.

**Kenneth Galbraith.** Mr. Ken Galbraith is the Managing Director of Five Corners Capital. He joined Ventures West as a General Partner in 2007 and led the firm's biotech practice prior to founding Five Corners Capital in 2013 to continue management of the Ventures West investment portfolio. Mr. Galbraith is a well-known and active member of the North American life sciences community with 30 years of experience acting as an executive, director, investor and advisor to companies in the biotechnology, medical device, pharmaceutical and healthcare sectors. Previously, Mr. Galbraith served as the Chairman and Interim CEO of AnorMED, a biopharmaceutical company focused on new therapeutic products in hematology, HIV and oncology, until its sale to Genzyme Corp. in a cash transaction worth almost US\$600 million. Starting in the biotech sector in 1987, Mr. Galbraith spent 13 years in senior

management with QLT Inc., a global biopharmaceutical company specializing in developing treatments for eye diseases and oncology, retiring in 2000 from his position as Executive VP and CFO when QLT's market capitalization exceeded US\$5 billion. He has served on the board of directors of several public and private biotechnology companies, including Zymeowrks, Angiotech Pharmaceuticals (ANPI), Aquinox (AQXP), Alder Pharmaceuticals (ALDR), Tekmira (TKMR) and Cardiome Pharma (CRME). He currently serves on the Board of Directors of MacroGenics (MGNX) and Profound Medical. Mr. Galbraith earned a Bachelor of Commerce (Honours) degree from the University of British Columbia in 1985 and appointed a Fellow of the Chartered Accountants of BC in 2013.

**Raymond Hakim.** Dr. Raymond M. Hakim, MD, PhD, FASN, is a Clinical Professor of Medicine at Vanderbilt University Medical Center since January 2011. Previously, Dr. Hakim served as Chief Medical Officer and Senior Executive Vice-President, Clinical and Scientific Affairs for Fresenius Medical Services, North America from 2007 to December 2011. Dr. Hakim started his career as an engineer, and received his PhD from Massachusetts Institute of Technology (MIT) in engineering in 1967 and worked as an engineer at Hydro-Québec until 1972. He attended McGill Medical School, completing his residency in internal medicine at the Royal Victoria Hospital in Montreal in 1979, and his Nephrology fellowship at Harvard Medical School and at Brigham and Women's Hospital in Boston, Massachusetts in 1981. From 1981 to 1987, he served on the faculty of Harvard University and was Associate Professor of Medicine and staff at the Brigham and Women's hospital. In 1987, Dr. Hakim began serving as Professor of Medicine and Director of the Clinical Division of Nephrology at the Vanderbilt University Medical School. He was also the Medical Director of the Vanderbilt Dialysis Unit. In 1995, Dr. Hakim became one of the founders of Renal Care Group, which grew to serve more than 35,000 patients and had the lowest standardized mortality among all dialysis providers. Renal Care Group, merged with Fresenius Medical Care, North America in 2007. Dr. Hakim has spoken at hundreds of patient and health care professional meetings and has authored more than 160 articles regarding issues in dialysis. He has also contributed chapters to more than 30 medical books. Dr. Hakim sits on the Public Policy Board of the American Society of Nephrology.

**Charles N. Kenworthy.** Mr. Charles N. Kenworthy is Executive Vice-President, Corporate Strategy, NantWorks, LLC since 2011. Mr. Kenworthy received his Bachelor of Arts from the University of California, Los Angeles, in 1980 and his Juris Doctorate from the University of San Diego School of Law in 1985. He joined the law firm of Allen Matkins in the mid-1980's and was a partner when he departed in 2006. Thereafter, he joined Abraxis Biosciences, LLC as Executive Vice-President, Corporate Strategy, at NantWorks, LLC.

**Louise Ménard.** Ms. Louise Ménard is President and director of Groupe Méfor Inc., a family holding Company since 1997. From August 2007 to October 2016, she served on the board of directors of the *Société des alcools du Québec* (SAQ) and was chair of its Governance Committee from 2007 to 2014, was a member of its Human Resources Committee from 2007 to 2016 and its Commercial Practices Committee from 2014 to 2016. Ms. Ménard also serves on the board of the directors of La Pièta since December 2012. From 2004 to 2007, Ms. Ménard served as board member of Comcorp Inc. (now Assuris Inc.), and was member of its Corporate Governance Committee and its Communications Committee. She also served on the board of directors of the Montreal Heart Institute Foundation from 1991 to 2006, and was a member of its Executive Committee from 1992 to 1998. From 2000 to 2002, she acted as Chairman of the board of directors of Alena Capital Inc. and from 1999 to 2001 she was on the board of directors of Bruneau Minerals Inc., a public company listed on the Montreal Stock Exchange. From 2003 to 2011, she was on the board of directors, and was a member of the Executive Committee (2003 and 2004) and the Corporate Governance Committee (2010) of On the Tip of the Toes Foundation and from 1988 to 1997, she was Vice president Legal Affairs of Sodarcac Inc., a public company listed on the TSX (now Aon Canada). She holds an LL.L from Université de Montréal (1973) and has graduated from the College of Directors of Laval University in 2009.

**Paul Mesburis.** Mr. Paul Mesburis is the Managing Principal of Empyrean Capital, and has more than twenty years of international experience in financial and capital markets. His capital markets experience encompasses senior roles for both buy-side and sell-side firms. On the buy-side, he has managed portfolios for global investment strategies in both debt and equities. On the sell-side, his experience includes senior roles in mergers and acquisitions, investment banking, and institutional equity research at HSBC Securities, Scotiabank Global Banking and Markets and Deutsche Bank Securities. His views on investments have been quoted in the media, including Report on Business of The Globe and Mail and the Financial Post, as well as the subject of features on BNN - Business News Network. In 2012, he was honoured with a Canadian Lipper Fund Award which recognizes funds that have excelled in delivering consistently strong risk-adjusted performance, relative to their peers. He received his Master of Business Administration degree from the Schulich School of Business at York University, his Bachelor of Arts degree from the University of Toronto, and has completed Executive Education at Harvard Business School. Mr. Mesburis holds the Chartered Professional Accountant (Ontario), Certified Public Accountant (Illinois) and Chartered Financial Analyst designations. He is a member of the Institute of Corporate Directors. Mr. Mesburis also serves on the board of directors and is the Chair of the Audit Committees of Avivagen Inc. and EEStor Corp. In addition, he is the Lead Director of Avivagen Inc. and Co-Chair of EEStor Corp.

**Nancy Orr.** Ms. Orr is a consultant with 30 years of experience in the development, financing and management of industrial projects, primarily in the energy and recycling sectors. She was President of Dynamis Group Inc., from 1991 to 2007, a private company that developed, built and operated cogeneration power plants and recycled paper and wood facilities. She has significant international experience, having worked in North Africa, Czech Republic, California, Spain, Ecuador and Canada. Throughout her career, Ms. Orr has served on several boards and audit committees of public, private and government entities. She has been a director and member of the audit committees of the Bank of Canada, Dundee Wealth Management Inc., Marleau, Lemire Securities, Fibrek Inc., Donohue Inc., HEC-Montreal and Redline Communications Inc., as well as a director of Palos Capital, Services Financiers de la Caisse de dépôt et placement du Québec, Socanav Inc., the Canada Arts Council Investment Committee and the Montreal Cardiology Institute. She graduated with a MBA from Queen's University in 1974 and a CA from McGill in 1977. She became a Fellow of the Quebec Order of Chartered Accountants in 1988. Ms. Orr currently sits on the board of directors of Mercer International Inc. and Ressources Quebec, a subsidiary of Les Investissements Quebec.

**Bruce Wendel.** Mr. Bruce Wendel is Chief Strategy Officer of Hepalink USA since June 2012. Mr. Wendel was Acting Chief Executive Officer of Scientific Protein Laboratories LLC from December 2014 to June 2015, a subsidiary of Shenzhen Hepalink Pharmaceutical CO., Ltd. From 2011 to 2012, he was consultant in the pharmaceutical industry. Mr. Wendel served as Vice Chairman and Chief Executive Officer of Abraxis BioScience until October 15, 2010, when Abraxis was acquired by Celgene Corporation. He was with Abraxis BioScience as of May 2006 and served as Executive Vice President of Corporate Development of Abraxis BioScience until being appointed as Executive Vice President of Corporate Operations and Development in November 2007. Mr. Wendel joined American Pharmaceutical Partners (APP) in 2004 as Vice President of Corporate Development. He began his 14 years with Bristol-Myers Squibb as in-house counsel before shifting to business and corporate development. Before joining APP, he served as Vice President, Business Development and Licensing for IVAX Corporation, a generic drug manufacturer. Previously, Mr. Wendel served in the legal departments of Playtex and Combe. He earned a Juris Doctorate degree from Georgetown University Law School, where he was an editor of Law and Policy in International Business, and a B.S. from Cornell University.

## Executive Officers

Executive Officers		
Name and Province or State and Country of Residence	Office held with the Corporation	With Prometic Since
<b>Pierre Laurin</b> Québec, Canada	President and Chief Executive Officer	1994
<b>Gregory Weaver</b> Massachusetts, USA	Chief Financial Officer	2015
<b>Bruce Pritchard</b> Hertfordshire, UK	Chief Operating Officer	2006
<b>Patrick Sartore</b> Québec, Canada	Chief Legal Officer and Corporate Secretary	2006
<b>John Moran</b> California, USA	Chief Medical Officer	2012

During the last five years, the above senior officers have held the position shown opposite their respective names or have occupied a management position with the same or a related entity except for (i) Mr. Gregory Weaver who was appointed Chief Financial Officer on November 1, 2015; (ii) Mr. Bruce Pritchard who was appointed Chief Operating Officer on August 12, 2014. Mr. Pritchard was previously Chief Financial Officer of the Corporation. He held both positions until he relinquished the position of Chief Financial Officer to Mr. Weaver; (iii) Dr. John Moran who was appointed on the Board of Directors in March 2012 and Chief Medical Officer of the Corporation on March 1, 2014; and (iv) Mr. Patrick Sartore who previously held the position of General Counsel and Corporate Secretary was appointed Chief Legal Officer and Corporate Secretary on May 13, 2015.

### Biographies

#### Executive Officers Who Also Serve as Directors

**Pierre Laurin, President and Chief Executive Officer.** Mr. Pierre Laurin is a senior executive with over 30 years of experience in the pharmaceutical and biotechnology industry. Involved in the development of Prometic's platform technology since 1989, Mr. Laurin founded Prometic Life Sciences Inc. in 1994. He served as Chairman until March 7, 2011 and President and Chief Executive Officer of the Corporation since its inception, he took the Corporation public on the TSX and has since raised over \$650 million through equity and debt financing and multinational funding. Mr. Laurin's corporate development achievements include the successful close of multiple licensing agreements and partnering agreements with multinationals, including two strategic agreements with the American Red Cross. Mr. Laurin's prior experience also includes positions with various pharmaceutical companies, including Nordic Laboratories (now Sanofi) where he played a pivotal role in the commercial success of Cardizem® in Canada. Mr. Laurin holds a B.Sc. in Pharmacy and a Masters degree in Pharmaceutical Sciences from the University of Montreal.

**John Moran, Chief Medical Officer.** Dr. John Moran MD, FRACP, FACP, FACPE, has served as Chief Medical Officer of Prometic since March 1, 2014. From 2010 until joining the Corporation, Dr. Moran was Vice President, Clinical Affairs - Home modalities at DaVita Healthcare Partners Inc. where he had the

overall responsibility for quality of care and related business issues for over 20,000 home dialysis patients in over 1,000 care centers. Previously, Dr. Moran served for eight years as Senior Vice President, Clinical Affairs for Satellite Healthcare. Dr. Moran also served for five years at Baxter Healthcare, as Global Medical Director for the Renal Division and for two years as Vice President for Clinical Development and Marketing.

#### *Executive Officers Who Do Not Serve as Directors*

**Gregory Weaver, Chief Financial Officer.** Mr. Greg Weaver joined the Corporation as Chief Financial Officer (“CFO”) in November 2015. Greg is an experienced CFO and board director, having served in executive positions with biopharma companies in the US and Europe. Most recently he served as CFO and board director with Oryzon Genomics in Boston and Barcelona, and previously has served as CFO with the following Nasdaq-listed public biotech companies: Fibrocell, Celsion, Poniard, Sirna, Nastech, and ILEX. Greg currently serves on the boards of US public biotech companies Egalet, and Atossa Genetics. Greg began his career as a CPA with Arthur Andersen, with an MBA from Boston College and BS in accounting from Trinity University.

**Bruce Pritchard, Chief Operating Officer.** Mr. Bruce Pritchard joined PLI as CFO of the UK subsidiary, Prometic BioSciences Ltd. (“PBL”) in 2006 and was promoted CFO of the group in 2008, relinquishing that post in November 2015. He became Chief Operating Officer in August 2014. He is a chartered accountant with many years of experience in general management, operations and corporate accountancy including senior finance positions with biotech and pharmaceutical companies. He has a proven track record of success in strategic acquisitions and in raising debt and equity finance. Mr. Pritchard is a Non-Executive Director and Chair of the Audit Committee of Imanova Limited. A Heriot-Watt University graduate, Mr. Pritchard gained a BA in Accountancy and Computer Science in 1993, he qualified as a Member of the Institute of Chartered Accountants of Scotland in 1996. He was appointed a Fellow of the Institute of Directors in 2014.

**Patrick Sartore, Chief Legal Officer and Corporate Secretary.** Mr. Patrick Sartore joined Prometic in 2006 as Senior Legal Counsel – Intellectual Property, was nominated Corporate Secretary of the Corporation in 2007. Mr. Sartore held the position of General Counsel and Corporate Secretary from May 2013 to May 2015, at which date he was appointed Chief Legal Officer and Corporate Secretary. Mr. Sartore was previously employed by Univalor Inc. as Legal Counsel and Leger Robic Richard, L.L.P., a firm specializing in Intellectual Property, Corporate and Commercial Law, as an associate attorney. Mr. Sartore has extensive experience in the areas of intellectual property, technology transfer, licensing and commercialization, private and public financing as well as general corporate and commercial law, namely in the biopharmaceutical field. Mr. Sartore graduated from the University of Montreal with a Bachelor of Law (LLB) in 1999 and was called to the Bar of Québec in 2001. Mr. Sartore also holds a Bachelor of Science, with Distinction, from Concordia University.

## **12.2. Independence**

As of March 23, 2017, all of the directors were “independent” in the meaning of Regulation 52-110 respecting Audit Committees except for:

- Mr. Pierre Laurin who is President and Chief Executive Officer of the Corporation.
- Mr. Stefan Clulow who was nominated by Structured Alpha to the Board, pursuant to the 2015 Amended and Restated Loan Agreements. Pursuant to the 2015 Amended and Restated Loan Agreements, Structured Alpha is entitled to nominate one person for election to the Board.
- Mr. Charles N. Kenworthy was nominated to the Board by California Capital Equity, LLC (“CCE”) (an affiliate of Abraxis Bioscience International Holding Company, Inc.), pursuant to a securities purchase agreement (the “Purchase Agreement”) entered into between the

Corporation and Abraxis Bioscience International Holding Company, Inc. on September 3, 2008. Pursuant to the Purchase Agreement, CCE is entitled to nominate one person for election to the Board.

- Dr. John Moran is Chief Medical Officer of the Corporation.
- Mr. Bruce Wendel was an employee of PBT, a wholly-owned subsidiary of the Corporation from April 1, 2012 to May 13, 2014, at which date his employment agreement terminated.

### 12.3. Security Holdings

As at March 23, 2017, the number and percentage of securities of Common Shares of the Corporation or its subsidiaries beneficially owned, directly or indirectly, or over which control or direction is exercised, by all directors and executive officers of the Corporation as a group is:

Securities	Number	Percentage of Class
Common Shares	17,303,884	2.59%

The information as to the number of Common Shares owned or over which control is exercised, not being within the knowledge of the Corporation, has been provided by each director and executive officer or is derived from insider reports.

### 12.4. Cease Trade Orders, Bankruptcies, Penalties or Sanctions

Except as indicated below, no director or executive officer of the Corporation:

- (a) is, as at the date hereof, or has been within the 10 years before the date hereof, a director, chief executive officer or chief financial officer of any company (including the Corporation) that:
  - (i) was the subject to an order that was issued while they were acting in the capacity of director, chief executive officer or chief financial officer; or
  - (ii) was subject to an order that was issued after they ceased to be a director, chief executive officer or chief financial officer and which resulted from an event that occurred while they were acting in the capacity of director, chief executive officer or chief financial officer.

Dr. Simon Best was Chairman of Ardana PLC, a publicly-traded company on the London Stock Exchange in the United Kingdom, which went into administration on June 30, 2008. The company was unable to complete refinancing or a possible sale or merger within a required timeframe. Concurrently, trading in the company's shares were suspended.

Ms. Nancy Orr was a director of Redline Communications Group Inc., a public company, from September 2008 to 2010 and interim CFO from September 2009 to 2010. In March 2010, it was determined that Redline had not followed proper accounting treatment. The company was therefore not in a position to issue its audited financial statements for the financial year ended December 31, 2009 and was obliged to restate its audited financial statements for the financial years 2007 and 2008. Between April 7, 2010 and June 23, 2010, the Ontario Securities Commission and the Autorité des Marchés Financiers issued several temporary cease trade orders. The last cease trade order was lifted on February 4, 2011.

Except as indicated below, no director or executive officer of the Corporation, or shareholder holding a sufficient number of securities of Prometic to affect materially the control of the Corporation:

- (a) is, as of the date hereof, or has been within the 10 years before the date hereof, a director or executive officer of any company (including the Corporation) that, while they were acting in that capacity,

or within a year of them ceasing to act in that capacity, became bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency or was subject to or instituted any proceedings, arrangement or compromise with creditors or had a receiver, receiver manager or trustee appointed to hold its assets; or

(b) has, within the 10 years before the date hereof, become bankrupt, made a proposal under any legislation relating to bankruptcy or insolvency, or become subject to or instituted any proceedings, arrangement or compromise with creditors, or had a receiver, receiver manager or trustee appointed to hold the assets of the director, executive officer or shareholder.

No director or executive officer of the Corporation, or shareholder holding a sufficient number of securities of the Corporation to affect materially the control of the Corporation has (i) been subject to any penalties or sanctions imposed by a court relating to securities legislation or by a securities regulatory authority; (ii) entered into a settlement agreement with a securities regulatory authority; or (iii) been subject to any other penalties or sanctions imposed by a court or regulatory body that would likely be considered material.

### **12.5. Conflicts of Interest**

To the knowledge of the Corporation, no director or executive officer of the Corporation has an existing or potential material conflict of interest with the Corporation or any of its subsidiaries, except for Mr. Pierre Laurin, Mr. Stefan Clulow, Mr. Charles Kenworthy, Dr. John Moran and Mr. Bruce Wendel, as disclosed under “Directors and Officers - Independence” and “Interest of Management and Others in Material Transactions”.

## **13. LEGAL PROCEEDINGS AND REGULATORY ACTIONS**

During the year ended December 31, 2012, the Corporation was served with a lawsuit in the Federal Court of Canada (Court) relating to a claim for infringement of two Canadian issued patents held by a third party plaintiff, GE Healthcare Biosciences AB (“**GE**”). The Corporation filed a statement of defence on the infringement claims, in addition to a counterclaim requesting that the Court declare both patents invalid and unenforceable.

During the 2016 Financial Year, the Corporation and GE entered into a settlement and license agreement (the “**Settlement Agreement**”) to mutually discontinue all past claims and counterclaims between the parties and to commercialize the underlying technologies over the term of the license, which shall not extend, on a country-by-country basis, beyond October 2021 (the “**Term**”). Under the terms of the Settlement Agreement, Prometic agreed to pay GE an aggregate amount of \$1M between October 25, 2016 and October 25, 2020 in consideration thereof, minimum annual royalty (“**MAR**”) payments totaling \$587,000 over the Term and a 2% net sales royalty on sales of certain Prometic bioseparation products to third parties and affiliates during the Term; the royalties being creditable against the MAR.

## **14. INTEREST OF MANAGEMENT AND OTHERS IN MATERIAL TRANSACTIONS**

On October 17, 2001, Mr. Pierre Laurin, President and Chief Executive Officer of the Corporation, via his company, Innovon Pharmaceuticals Inc. (“**Innovon**”) entered into an assignment agreement with the Corporation whereby rights to PBI-1402 and PBI-1101 were assigned to the Corporation. Pursuant to said agreement, Mr. Laurin, via Innovon, is entitled to receive royalties based on the sales of PBI-1402, PBI-1101 as well as any analogs thereof (eg. PBI-4050). These royalties consist of 0.5% of net sales from direct or indirect sales by the Corporation or its affiliates or 3% of revenues received by PBI from third parties for such products.

Moreover, 450,000 shares were placed in escrow with Computershare Trust Company of Canada, as escrow agent, by Mr. Pierre Laurin, President and Chief Executive Officer of the Corporation, as security



for a loan by the Corporation in the amount of \$450,000 granted in order to enable Mr. Laurin to exercise options to acquire Common Shares. Mr. Laurin repaid 105,133 which was applied against accumulated interest, making the amount owed as of March 23, 2017 equal to \$400,000. The loan was last amended on February 25, 2016. The February 25, 2016 amendment provides for the loan to bear interest at a rate equal to the Bank of Canada's prime rate plus 1% per annum and stipulates that the loan is repayable upon the earlier of (i) March 31, 2019 or (ii) thirty (30) days preceding a targeted NASDAQ or NYSE listing date of the Common Shares.

## **15. TRANSFER AGENT AND REGISTRAR**

The Corporation's transfer agent and registrar is Computershare Trust Company of Canada, 100 University Avenue, 9th Floor, North Tower, Toronto, Ontario M5J 2Y1, and the registers of transfers of each class of securities are located in Montréal, Québec and Toronto, Ontario.

## **16. MATERIAL CONTRACTS**

Except for those contracts entered into in the ordinary course of business, the following material contracts of the Corporation were either entered into within the last financial year or before the last financial year but are still in effect as of the date hereof:

### *Pierre Laurin*

- The Amended and Restated Loan Agreement dated February 25, 2016 between Prometic and Mr. Pierre Laurin, President and CEO of Prometic. See under section 14 - "Interest of Management and Others in Material Transactions" above for further details.

### *Structured Alpha (an affiliate of Thomvest Seed Capital Inc)*

- The Third Amended and Restated Loan Agreement originally dated as of September 10, 2013, as amended and restated pursuant to the first amendment on July 31, 2014, as further amended and restated pursuant to the second amendment on March 31, 2015 and as further amended and restated pursuant to the third amendment on February 29, 2016 between, among others, Prometic and Structured Alpha, and providing for an original issue discount loan in the principal amount of \$10 million.
- The Second Amended and Restated Loan Agreement originally dated as of July 31, 2014, as amended and restated pursuant to the first amendment on March 31, 2015, and as further amended and restated pursuant to the second amendment on February 29, 2016 between, among others, Prometic and Structured Alpha, and providing for an original issue discount loan in the principal amount of \$20 million.

### *RBC Dominion Securities Inc., Canaccord Genuity Corp., et al.*

- Underwriting Agreement dated May 10, 2016 between Prometic and RBC Dominion Securities Inc., Canaccord Genuity Corp. (together, the Lead Underwriters), Scotia Capital Inc., CIBC World Markets Inc., National Bank Financial Inc., Paradigm Capital Inc. and Beacon Securities Limited.

## **17. INTERESTS OF EXPERTS**

### **Names of Experts**

The consolidated annual financial statements of the Corporation for the 2016 Financial Year included in the Corporation's 2016 Annual Report have been audited by Ernst & Young LLP.

## Interests of Experts

None of Ernst & Young LLP or its partners hold any registered or beneficial interests, directly or indirectly, in the securities of the Corporation or its associates or affiliates, and is independent of the Corporation within the meaning of the Code of Ethics of the *Ordre des comptables professionnels du Québec*.

## 18. AUDIT & RISK COMMITTEE

### Audit & Risk Committee Charter

The Corporation's Audit & Risk Committee Charter is reproduced at Appendix A.

### Composition

The Audit & Risk Committee is composed of four independent and financially literate directors: its chair, Mr. Paul Mesburis, Prof. Simon Best, Mr. Andrew Bishop and Ms. Nancy Orr.

### Relevant Education and Experience

Member	Relevant Education and Experience
Mr. Paul Mesburis	<ul style="list-style-type: none"><li>Mr. Mesburis is a Chartered Professional Accountant (Ontario), Certified Public Accountant (Illinois) and a Chartered Financial Analyst. He earned his MBA from the Schulich School of Business at York University and a B.A. from the University of Toronto.</li><li>He has more than 20 years of experience in the financial services industry. His capital markets experience encompasses roles for both buy-side and sell-side firms.</li><li>On the buy-side, he has managed portfolios for global investment strategies in both debt and equities.</li><li>On the sell-side, his experience includes senior roles in mergers and acquisitions, investment banking, and institutional equity research at HSBC Securities, Scotiabank Global Banking and Markets and Deutsche Bank Securities.</li><li>He has served as a Board member and Audit Committee member of other public and private companies.</li></ul>
Prof. Simon Best	<ul style="list-style-type: none"><li>Prof. Best received an M.B.A. in 1985 from London Business School.</li><li>He served as Chairman of Ardana PLC, a UK company listed on the London Stock Exchange, for three years as well as Board member and Audit Committee member on other public and private companies.</li></ul>

Member	Relevant Education and Experience
Mr. Andrew Bishop	<ul style="list-style-type: none"> <li>○ Mr. Andrew Bishop received an M.B.A. in 1993 (with distinction) from the Schulich School of Business at York University. He also received his Chartered Financial Analyst designation in 2001.</li> <li>○ He has over 20 years of experience in investment banking and private equity. Over his career, he has evaluated many financial situations including over 100 financing and M&amp;A transactions. He also has worked closely in the preparation of financial statements for corporations, limited partnerships and non-for-profits.</li> <li>○ He serves as Acting Chief Financial Officer for Arch Biopartners, a public company listed on the TSXV. He has served as member of the Audit Committee of several private and non-for-profit companies.</li> </ul>
Ms. Nancy Orr	<ul style="list-style-type: none"> <li>○ Ms. Orr received an M.B.A. from Queen's University and a C.A. from McGill University and she has been a Fellow of the Québec Order of Chartered Accountants since 1988.</li> <li>○ She has substantial experience as a member of several boards of directors and audit committees of public, private and government entities.</li> </ul>

***Audit & Risk Committee Oversight***

Since January 1, 2014, all recommendations of the Audit & Risk Committee to nominate or compensate external auditors were adopted by the Board of Directors.

***Pre-Approval Policies and Procedures***

The Audit & Risk Committee has reviewed and approved non-audit services on a case-by-case basis throughout the 2016 Financial Year.

**19. EXTERNAL AUDITOR SERVICES FEES**

Ernst & Young LLP have served as the Corporation's auditors since financial year 2010.

**Audit Fees**

Ernst & Young LLP provided services and billed the Corporation and its subsidiaries \$489,600 for professional services rendered for 2016 Financial Year (\$605,000 for the 2015 Financial Year) in relation to the audit of the Corporation's financial statements, statutory audits of subsidiaries as well as in relation to quarterly reviews and short-form prospectus.

**Audit-Related Fees**

Ernst & Young LLP did not provide any audit-related services to the Corporation for 2016 Financial Year. Ernst & Young LLP provided services and billed the Corporation \$1,700 for 2015 Financial Year for audit-related services, such as consultations related to accounting and reporting matters.

**Tax Fees**

Ernst & Young LLP provided services and billed the Corporation \$58,400 for 2016 Financial Year (nil for 2015 Financial Year) for tax compliance, advice or planning services.

**All Other Fees**

Ernst & Young LLP provided services and billed the Corporation \$38,800 for 2016 Financial Year (\$37,600 for 2015 Financial Year) for translation services.

**20. ADDITIONAL INFORMATION**

Additional information relating to the Corporation may also be found on the SEDAR website at [www.sedar.com](http://www.sedar.com) or on the Corporation's website at [www.Prometic.com](http://www.Prometic.com).

Additional information including directors' and officers' remuneration and indebtedness, principal holders of the Corporation's securities and securities authorized for issuance under equity compensation plans, is contained in the Corporation's Management Information Circular for its most recent annual meeting of shareholders that involved the election of directors.

Additional financial information is provided in the Corporation's financial statements and management's discussion and analysis for its most recently completed financial year.

## APPENDIX A

### Audit & Risk Committee Charter

#### I. PURPOSE

The Board of Directors of Prometic Life Sciences Inc. (the “Corporation”) is ultimately responsible for the stewardship of the Corporation, which means that it oversees the day-to-day management delegated to the President and Chief Executive Officer and the other officers of the Corporation. The Audit & Risk Committee (the “Committee”) is appointed by the Board of Directors to assist the Board in fulfilling this responsibility with respect to overseeing four (4) fundamental issues: (i) the Corporation’s financial reporting process and internal control systems, (ii) the Corporation’s process to identify and manage risks, (iii) the internal and external audit process; and (iv) the Corporation’s communication system to provide an open avenue of communication among the external auditors, the financial and senior management, the internal auditing department (if any), and the Board of Directors.

#### II. GENERAL ROLE AND MANDATE

##### External Auditors

1. Review the independence and the performance of the external auditors.
2. Recommend to the Board of Directors the appointment of the external auditors, to be approved by the shareholders, for the purpose of preparing or issuing an auditor’s report or performing other audit, review or attest services for the Corporation or the approval of any discharge of auditors where circumstances warrant.
3. Recommend to the Board of Directors for approval the fees and other compensation to be paid to the external auditors.
4. Pre-approve non-audit services to be provided to the Corporation or its subsidiaries by the external auditors, other than non-audit services: (i) that were not recognized as non-audit services at the time of the engagement and (ii) that are promptly brought to the attention of the Committee and approved, prior to the completion of the audit, by the Committee or by one or more of its members to whom authority to grant such approvals has been delegated by the Committee.
5. Oversee the work of the external auditor engaged for the purpose of preparing or issuing an auditor’s report or performing other audit, review or attest services for the Corporation, review the external auditors’ audit plan, discuss and approve audit scope, reliance upon management and internal audit if or when applicable, and general audit approach. At the conclusion of the audit process, and before releasing the year-end earnings, discuss the results of such audit with the external auditors including the resolution of disagreements between management and the external auditor regarding financial reporting and difficulties encountered in performing the audit.
6. Discuss with the auditors the quality and not just the acceptability of the Corporation’s accounting principles including all critical accounting policies and practices used, any alternate treatments of financial information that have been discussed with management, the ramification of their use and the auditor’s preferred treatment, as well as any other material communications with management.
7. The external auditors report to and are accountable to the Committee and the Board of Directors as representatives of shareholders.

##### Internal Auditors

8. Assess with management the need for internal audit as circumstances facing the Corporation change.

9. Review and approve management's decisions related to the need for internal auditing.
10. Review the mandate, budget plan, organizational structure and qualification of the internal audit department as needed.

#### Financial Reporting and Risk Management

11. Review the quarterly Management Accounts pack of the Corporation, understanding the key variances from budget and the impact on the cash flow of the Corporation.
12. Consider and review with the external and internal auditors, if or when applicable, the integrity of the Corporation's financial reporting processes, both internal and external, and the adequacy of the Corporation's internal controls and management financial information systems.
13. On an annual basis, review and discuss with management and the external auditors, significant risks and exposures, the steps management has taken to monitor, control and report such risks and exposures, and the effectiveness of the overall process for identifying the principal financial risks affecting financial report.
14. Review and discuss with management and the external auditors (including the internal auditors if any) the Corporation's audited annual financial statements, any other financial statements to be audited, non-audited interim financial statements, management discussion and analysis and all other public disclosure documents containing material financial information, and make recommendations for their approval by the Board of Directors, prior to filing or distribution. The review should include a discussion with management and the external auditors of significant issues regarding accounting principles, practices and significant management estimates and judgments.
15. Ensure that adequate procedures are in place for the review of the Corporation's public disclosure of financial information extracted or derived from its financial statements, other than the public disclosures referred to in paragraph 14 above, and periodically assess the adequacy of those procedures.
16. Review, with the Corporation's counsel, any legal or regulatory matter that could have a significant impact on the Corporation's financial statements.
17. Review and make recommendations with respect to any litigation, claim or contingency that could have a material effect upon the financial position of the Corporation and the appropriateness of the disclosure thereof in the documents reviewed by the Committee.
18. Establish procedures for:
  - (a) the receipt, retention and treatment of complaints received by the Corporation regarding accounting, internal accounting controls, or auditing matters; and
  - (b) the confidential, anonymous submission by employees of the Corporation of concerns regarding questionable accounting or auditing matters.
19. Review the CEO/CFO's report disclosing any fraud involving management or other employees who have a significant role in the issuer's ICFR52-109.
20. Review, if applicable, the monitoring reports from the Chair of the Corporate Governance Committee and the Chair of the Audit & Risk Committee, pursuant to the Corporation's Whistleblower policy.
21. Review and make recommendation regarding insurance coverage (annually or as may be otherwise appropriate).

22. Review and approve the Corporation's hiring policies regarding partners, employees and former partners and employees of present and former external auditors of the Corporation.

23. Review the Corporations Table of Authority and recommend any amendments to the Board of Directors for approval.

Other

24. Determine the appropriateness of declaring dividends.

25. Review the Corporation's Annual Information Form and recommend its approval to the Board of Directors.

26. Review the Annual Budget of the Corporation and recommend its approval to the Board of Directors.

27. Review and approve guidelines and policies for Treasury and Foreign Exchange operations within the group.

28. Perform any other activities consistent with its responsibilities and duties, the Corporation's by-laws and governing law as the Committee or the Board of Directors deems necessary or appropriate.

29. Keep records of its activities, meetings, etc. at the office of the Corporate Secretary and report periodically to the Board of Directors on its activities and make recommendations as deemed appropriate.

30. Establish and monitor performance against an Annual Workplan to monitor and ensure compliance with the Charter of the Audit & Risk Committee.

31. Annually assess the effectiveness of the Committee against its general role and mandate (charter) and report the results of the assessment to the Board of Directors.

32. Review and, if necessary recommend to the Board of Directors, any update to the Charter of the Audit & Risk Committee.

33. Approve the hiring of the Chief Financial Officer and other senior management officers whose principal duties and responsibilities relate directly to the finances of the Corporation.

The Audit & Risk Committee may:

(a) with the approval of the Board of Directors and at the Corporation's expense engage independent counsel and other external advisors as it determines necessary to carry out its duties;

(b) set and pay the compensation for any such advisors employed by the Committee; and

(c) communicate directly with the internal and external auditors.

### III. COMPOSITION

The Audit & Risk Committee shall be comprised of a minimum of three (3) and a maximum of six (6) independent directors of the Corporation, appointed by the Board of Directors following the Annual General Meeting to serve on the Committee until the close of the next annual meeting of shareholders of the Corporation or until the member ceases to be a director, resigns or is replaced, whichever first occurs. Any member may be removed from office or replaced at any time by the Board of Directors.

A member of the Committee is independent if the member has no material relationship with the Corporation, within the meaning of Regulation 52-110 respecting Audit Committees as amended from time to time.

Unless a chairman is elected by the full Board of Directors, or if not present at the meeting, the members of the Audit & Risk Committee may designate a chairman by majority vote of the full Audit & Risk Committee membership.

All members of the Audit & Risk Committee shall be financially literate, that being defined as able to read and understand a set of financial statements that present a breadth and level of complexity of accounting issues that are generally comparable to the breadth and complexity of the issues that can reasonably be expected to be raised by the Corporation's financial statement. However, a member who is not financially literate may be appointed to the Committee provided that the member becomes financially literate within a reasonable period of time following his or her appointment. At least one member should have accounting or related financial experience and the ability to analyze and interpret a full set of financial statements, including the notes attached thereto, in accordance with International Financial Reporting Standards (IFRS).

#### IV. MEETINGS

The Committee shall meet at least four (4) times annually, or more frequently as circumstances dictate. The Committee may ask members of management or others to attend meetings and provide pertinent information as required. Quorum for all meetings will consist of at least two (2) members.

The Committee's Chair shall prepare an agenda in advance of each meeting in consultation with management and the other members of the Committee. External auditors may also be consulted for any item related to their responsibilities and duties.

The Committee may meet with the external auditors, in private, at least once during the year. The Committee may also communicate with management and external auditors, if deemed necessary, on a quarterly basis to review the Corporation's interim financial statements.

#### V. WORK PROGRAM

The Audit & Risk Committee annually establishes a work program in order to fix a schedule to fulfill its responsibilities pursuant to the content of this charter. The Committee uses such work program, inter alia, to evaluate its compliance with this charter.

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