



**NUVO RESEARCH INC.**

**ANNUAL INFORMATION FORM**

**February 26, 2009**

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## **CERTAIN REFERENCES**

Unless otherwise noted, the information contained in this Annual Information Form (“AIF”) is provided as at December 31, 2008 or for the period ended December 31, 2008 as applicable.

For an explanation of the capitalized terms and expressions, please refer to the “Glossary of Terms” at the end of this AIF. Unless otherwise noted, or indicated by context, “Nuvo Research Inc.”, “Dimethaid Research Inc.”, “Nuvo”, the “Corporation” and “we” refer to Nuvo Research Inc. and its direct and indirect subsidiaries.

All dollar amounts are expressed in Canadian dollars unless otherwise noted.

## **FORWARD-LOOKING INFORMATION**

Certain statements made in this AIF may constitute “forward-looking” statements involving known and unknown risks, uncertainties and other factors (including, but not limited to, the factors discussed under “Risk Factors”) that may cause actual results, performance or achievements, or industry results, to differ materially from any future results, performance or achievements expressed or implied. Forward-looking statements should not be read as guarantees of future performance or results, and they will not necessarily be accurate indications of whether such results will be achieved. We use words such as “may”, “would”, “could”, “will”, “likely”, “expect”, “anticipate”, “believe”, “intend”, “plan”, “forecast”, “project”, “estimate” and similar expressions to identify forward-looking statements.

Although the forward-looking statements in this AIF are based upon what we believe to be reasonable assumptions, we cannot assure investors that actual results will be consistent with these statements. They reflect current expectations of future events on the date of this AIF. The Corporation assumes no obligation to update or revise forward-looking statements.

## **NUVO RESEARCH INC. STRUCTURE**

### **Corporate Structure**

Nuvo Research Inc. was incorporated on August 22, 1983 under the laws of the Province of Ontario as Clark Pharmaceutical Laboratories Ltd. On November 14, 1990, the articles were amended to change the name of the Corporation from Clark Pharmaceutical Laboratories Ltd. to Dimethaid Research Inc. On September 30, 2005, the articles were further amended to change the name of the Corporation from Dimethaid Research Inc. to Nuvo Research Inc. On January 1, 2007, the Corporation completed a short-form amalgamation with Akorn Pharmaceuticals Canada Limited, Excelpharm Inc., Femina Inc., Dimethaid Management Inc. and Dimethaid Manufacturing Inc., certain of its subsidiaries. The amalgamated entity continues as Nuvo Research Inc. No new securities of the Corporation were issued in connection with the amalgamation and securities of the Corporation prior to the amalgamation continue to represent securities of the amalgamated entity.

The Corporation’s registered office and principal place of business is located at 7560 Airport Road, Unit 10, Mississauga, Ontario L4T 4H4. The Corporation’s telephone number is (905) 673-6980 and its web address is [www.nuvoresearch.com](http://www.nuvoresearch.com). The Corporation also operates a division in Varennes, Québec where it manufactures Pennsaid®.

***Akorn Pharmaceuticals Canada Limited (“Akorn”)***

In September 1992, the Corporation acquired Akorn, which carried on business as Dioptic Laboratories (“Dioptic”). Through Akorn, the Corporation distributed branded, diagnostic and therapeutic ophthalmic products in Canada. In the fall of 2005, the Corporation completed the sale of Akorn’s principal assets and Akorn discontinued all operations. (See “General Development of the Business – Dispositions”). On January 1, 2007, Akorn amalgamated with Nuvo as part of the amalgamation described above under “Corporate Structure”.

***Dimethaid Management Inc. (“DMgmt”)***

In March 1993, DMgmt was incorporated as a wholly owned subsidiary of the Corporation. It owned the lands and building at 1405 Denison Street, Markham, Ontario, where the Corporation’s head office was formerly located. On January 6, 2006, the Corporation completed the sale of such lands and building for a total purchase price of \$2.9 million. The Corporation continued to occupy the property pursuant to a short-term lease with the purchaser of the property until March 2006, at which time it moved to leased facilities located at 7560 Airport Road, Unit 10, Mississauga, Ontario. (See “General Development of the Business – Dispositions”). On January 1, 2007, DMgmt amalgamated with Nuvo as part of the amalgamation described above under “Corporate Structure”.

***Dimethaid Immunology Inc. (“Dimethaid Immunology”)***

In June 1993, Dimethaid Immunology was incorporated as a wholly owned subsidiary of the Corporation. It was responsible for the Canadian marketing and distribution of WF10, an aqueous solution of OXO-K993, containing stabilized chlorite ions, as well as related products developed by Oxo Chemie AG of Switzerland (“Oxo Chemie”). Oxo Chemie (now Dimethaid AG) was purchased by the Corporation in May 2002. (See “– Dimethaid AG, Dimethaid GmbH and Nuvo Research GmbH” and “General Development of the Business – Acquisitions – Oxo Chemie AG”). Dimethaid Immunology currently has limited activity since WF10 and related products are not currently approved for sale in Canada.

***Dimethaid International Inc., Dimethaid (UK) Ltd. and Dimethaid S.V. Inc.***

In May 1997, the Corporation transferred the non-Canadian patents, technology, trademarks and other intellectual property rights related to its then existing transdermal drug delivery system to a newly incorporated wholly owned Barbados subsidiary, Dimethaid International Inc. (“International”). International’s mandate was to commercialize products that emanated from these intellectual property rights. International had two wholly owned subsidiaries, Dimethaid (UK) Ltd. and Dimethaid S.V. Inc. Dimethaid (UK) Ltd. is a British company incorporated in 1999 that holds the marketing authorization for Pennsaid® in the United Kingdom. Dimethaid S.V. Inc. was a St. Vincent company incorporated in 2001 that held the rights to distribute Pennsaid® in the Caribbean. In December 2007, Dimethaid S.V. Inc. was liquidated and voluntarily wound up into International. Concurrently, International applied to the Registrar of Companies in Barbados under section 356.4 of the Companies Act to continue as a corporation in another jurisdiction and was continued under the Canada Business Corporations Act. International conveyed all of its assets to its parent company Nuvo and Nuvo assumed all of its liabilities whereupon International was subsequently dissolved. Dimethaid (UK) Ltd. is now a wholly owned subsidiary of Nuvo Research Inc.

### ***Dimethaid Health Care Ltd. (“DHCL”)***

In November 1998, Dimethaid Operations Inc., a wholly owned subsidiary of the Corporation, was continued under the Canadian Business Corporations Act as Dimethaid Health Care Ltd. Its mandate was to develop and commercialize Pennsaid® for the Canadian market. In August of 2005, DHCL was sold to Paladin Labs Inc. (“Paladin”) and its name was subsequently changed to Squire Pharmaceuticals Inc. (“Squire”) (See “General Development of the Business – Products – Pennsaid®” and “General Development of the Business – Dispositions”).

### ***Dimethaid Manufacturing Inc. (“DMI”)***

In February 2000, DMI was incorporated as a wholly owned subsidiary of the Corporation under the Canadian Business Corporations Act. DMI owned a manufacturing facility in Varennes, Québec where it manufactured Pennsaid®. In December 2006, DMI was continued under the Ontario Business Corporations Act and on January 1, 2007, DMI amalgamated with Nuvo as part of the amalgamation described previously under “Corporate Structure”. In connection with the amalgamation, Nuvo registered the trade names Nuvo Manufacturing and Fabrication Nuvo. The Varennes manufacturing facility now operates as Nuvo Manufacturing (Fabrication Nuvo), a division of the Corporation.

### ***Dimethaid AG, Dimethaid GmbH and Nuvo Research GmbH***

In May 2002, the Corporation completed the acquisition from Dr. F.W. Kühne of Oxo Chemie. Oxo Chemie was a Swiss company headquartered in Fribourg, Switzerland that owned the intellectual property rights relating to WF10. The assets acquired by Nuvo included an OXO-K993 manufacturing plant, equipment and inventory in Wanzleben, Germany and the marketing rights for WF10 in Thailand. (See “Narrative Description of the Business – Intellectual Property”). OXO-K993, a stabilized chlorite ion solution is used to produce WF10 and Oxoferin™.

Upon completing the acquisition of Oxo Chemie it was restructured into Dimethaid AG, Dimethaid GmbH and Dimethaid (Thailand) Limited. Dimethaid AG retained all rights relating to the WF10 patents and intellectual property. Dimethaid GmbH was incorporated as a new, wholly owned German subsidiary of the Corporation overseeing the OXO-K993 manufacturing facilities in Wanzleben. Dimethaid (Thailand) Limited was registered in Thailand as a wholly owned subsidiary of Nuvo, with the intent of exploiting WF10 marketing rights in that country.

In November 2004, the Corporation restructured its relationship with Dr. Kühne and entered into an agreement effective May 31, 2005, to reflect these restructured arrangements. Pursuant to this new agreement, the Corporation transferred all shares of Dimethaid GmbH to Dimethaid AG, making Dimethaid GmbH a wholly owned subsidiary of Dimethaid AG. Dimethaid (Thailand) Limited, which never commenced operations, transferred its WF10 marketing rights for Thailand to Dr. Kühne and the Corporation transferred a 40% ownership interest in Dimethaid AG to Dr. Kühne. (See “General Development of the Business – Acquisitions – Oxo Chemie AG”).

In 2007, Dimethaid (Thailand) Limited was dissolved.

In July 2008, Dimethaid AG established a wholly owned subsidiary Nuvo Research GmbH (“NRG”). NRG’s office and operations are located in Leipzig, Germany. It will conduct

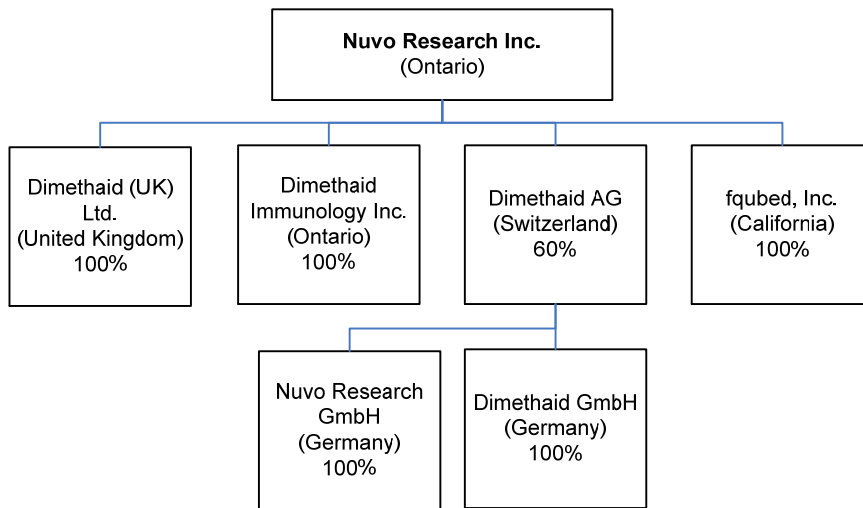
and co-ordinate certain future research and development activities related to WF10 including arranging the necessary funding to conduct such research and development.

***fqubed, Inc.***

In December 2005, the Corporation acquired all of the common shares of fqubed, Inc. (“fqubed”), a company based in San Diego, California. Initially using technology licensed from the University of California, fqubed has developed proprietary screening capabilities to identify innovative formulations that can efficiently deliver active therapeutics into and through the skin. Nuvo is using this technology to expand its pipeline of topically and transdermally delivered therapeutics. (See “General Development of the Business – Acquisitions – fqubed”).

**Organizational Chart**

The following chart illustrates Nuvo’s relationship to its subsidiaries as at December 31, 2008, indicates their respective jurisdictions of incorporation, as well as the percentage ownership.



## GENERAL DEVELOPMENT OF THE BUSINESS

Nuvo is a Canadian drug development company primarily focused on the research and development of drug products that are delivered to and through the skin. Nuvo is also involved in research and development activities involving WF10, a chlorite-based, immunomodulating drug through its 60% interest in Dimethaid AG. The Corporation refers to and manages these activities as two distinct business or research segments: (i) topical and transdermal drug delivery; and (ii) immune system regulation.

### Strategy

The Corporation's long-term strategy is to build a profitable company focused on pharmaceutical research and development ("R&D") and early to mid-stage drug development.

On September 21, 2004, following a proxy contest, the Corporation's shareholders elected a new Board of Directors, and on September 22, 2004, the Board appointed a new president and chief executive officer, Dr. Henrich Guntermann.

Following its election, the Board and management adopted a new strategy that it believed would improve the Corporation's performance. Prior to September 22, 2004, the business of the Corporation was focused on establishing a "fully integrated" pharmaceutical company, which assumed complete responsibility for the discovery, development, commercialization, marketing (in some jurisdictions) and manufacturing of all drug candidates. The new business plan narrowed the Corporation's focus to early to mid-stage drug development activities, from discovery through formulation and early stage clinical development, with the goal of outlicensing drug candidates at various stages of development prior to regulatory approval.

To support this new targeted focus, the Corporation has since:

- developed a new formulation for its lead product, Pennsaid®. This formulation, called Pennsaid® Plus, is designed to provide users with the efficacy of existing Pennsaid®, combined with less frequent dosing and increased ease of application. Patent applications for Pennsaid® Plus have been filed. If the patents are granted, a level of patent protection currently lacking for the original Pennsaid® would be established. The Corporation does not plan to initiate the pivotal phase 3 trials for Pennsaid® Plus until certain goals are achieved including receipt of sufficient funds to complete the trials;
- created Scientific and Pain Products Advisory Boards consisting of renowned scientists, researchers, doctors and regulatory experts who can advise and assist management in the evaluation of potential drug candidates, drug development plans and specific issues relating to the Corporation's business;
- strengthened the management and scientific teams through the recruitment or promotion of qualified executives for key new roles such as Vice President, Pain Products, Vice President, New Product Planning, and Chief Intellectual Property Counsel, the hiring of new staff into existing roles and by acquiring fqubed and expanding its scientific team in San Diego;

- retained licensing and commercialization consultants to assist the Corporation in forming drug development and pharmaceutical marketing partnerships. The Corporation is in various stages of licensing discussions with pharmaceutical companies possessing sales and distribution capabilities for the marketing of Pennsaid® and Pennsaid® Plus in the United States and other territories; and,
- retained several regulatory and chemistry, manufacturing and controls (“CMC”) consultants with FDA experience to assist the Corporation in obtaining regulatory approval for its products, in particular, FDA approval for the sale and marketing of Pennsaid® in the United States.

## **Products**

### ***Pennsaid®***

Pennsaid®, the Corporation’s lead product, is used to treat the pain and symptoms associated with knee osteoarthritis (“OA”). OA is the most common joint disease affecting middle-age and older people. It is characterized by progressive damage to the joint cartilage and causes changes in the structures around the joint. These changes can include fluid accumulation, bony overgrowth, and loosening and weakness of muscles and tendons, all of which may limit movement and cause pain and swelling.

Pennsaid® combines a transdermal carrier (containing dimethyl sulfoxide, popularly known as “DMSO”) with diclofenac sodium, a leading non-steroidal anti-inflammatory drug (“NSAID”), and delivers the active drug through the skin directly to the site of pain. While, conventional oral NSAIDs expose patients to potentially serious systemic side effects such as gastrointestinal bleeding and cardiovascular risks, Nuvo’s clinical trials suggest that some of these systemic side effects occur less frequently with topically applied Pennsaid®.

Nuvo does not directly market Pennsaid® in jurisdictions where the product has been approved. Instead, it enters into marketing and/or distribution agreements with third-party partners that have sales and marketing capabilities. Pennsaid® has been approved for marketing and sale in a number of countries, including Canada, several Caribbean nations and a number of European countries including Greece, Italy and the United Kingdom. It has not received FDA approval allowing it to be marketed and sold in the United States.

Until August 16, 2005, the Corporation’s wholly owned subsidiary, DHCL, had the exclusive right to distribute Pennsaid® in Canada. On August 16, 2005, DHCL was sold to Paladin in consideration for upfront payments totalling \$7.5 million, plus a long-term agreement calling for Nuvo to continue supplying Pennsaid® for the Canadian market through the Corporation’s manufacturing facility in Varennes Quebec, which at the time was owned by the Corporation’s subsidiary, DMI (see “Corporate Structure”). The agreement also provided that the Corporation would continue to share in certain future operating revenues arising from Canadian Pennsaid® sales in excess of target amounts until 2014. On January 16, 2006, rights to certain residual Canadian Pennsaid® sales revenues retained by the Corporation were transferred to Squire, which was then a wholly owned subsidiary of Paladin, in consideration of an upfront \$3.25-million payment and future Canadian sales royalties. On July 7, 2008, the Corporation and Squire reached an agreement to amend and restate the Pennsaid® and Pennsaid® Plus licensing, supply and other arrangements in exchange for payments totalling \$2.5 million by Squire to the Corporation, including \$0.6 million in full settlement of amounts receivable relating to Ontario Innovation Tax Credits, \$0.9 million to settle obligations under the original licensing arrangements and \$1.0 million as a prepayment of future royalties that would

otherwise be payable by Paladin to the Corporation through December 31, 2010 (the “Amended and Restated Canadian Licensing Arrangements”). Under the terms of the Amended and Restated Canadian Licensing Arrangements, the Term was increased to 99 years and now ends in August 2104. As part of the new arrangements the Corporation relinquished the right to share in certain future operating revenues in excess of target amounts. However, effective January 1, 2011 and until the end of the Term, Squire will pay the Corporation a royalty based upon Canadian sales of Pennsaid®.

As a result of these arrangements, since August 16, 2005, the Corporation’s revenues have not included sales revenue from the sale of Pennsaid® in Canada for retail distribution, but have included contract manufacturing revenue from the manufacture and supply of Pennsaid® to Squire, a share of Canadian revenues above specified targets under the original agreements and systematically amortized portions of the upfront payments. Commencing January 2011, the Corporation’s revenues will also include a royalty based on Canadian sales of Pennsaid® (See “—Recent Financings and Corporate Transactions”).

The Corporation’s initial submission for FDA approval to market Pennsaid® in the United States was made in 2001. In August 2002, in response to the Corporation’s initial new drug application (“NDA”) application for Pennsaid®, the FDA sent the Corporation a non-approvable letter (the “Non-Approvable Letter”), detailing a number of deficiencies in the Corporation’s application. In consultation with the FDA, the Corporation designed two new Phase 3 clinical trials, a 12-week efficacy trial and a long-term safety trial and conducted a pharmacokinetic study providing more information on DMSO in order to address the deficiencies cited by the FDA in the Non-Approvable Letter. The Corporation successfully completed all required trials and submitted an NDA to the FDA in June 2006.

On December 28, 2006, Nuvo received an approvable letter from the FDA for Pennsaid® (the “Approvable Letter”). In its letter, the FDA indicated that Pennsaid® is approvable subject to Nuvo satisfying certain conditions including the provision of additional nonclinical dermal safety and packaging data. None of the conditions in the Approvable Letter related to the clinical efficacy or the clinical safety of Pennsaid®. Furthermore, none of these conditions had been raised by the FDA in the Non-Approvable Letter of August 2002. The FDA has not requested that Nuvo conduct any additional Phase 3 clinical trials as a condition of approval.

During 2007 the Corporation engaged in communications with the FDA in an effort to clarify the Agency’s expectations as outlined in the Approvable Letter. Through these communications the FDA clarified certain of its requirements for additional information relating to Pennsaid®. Based on the contents of the Approvable Letter and these clarifications, the Corporation completed several short-term studies (the “Short-Term Studies”). In addition, the Corporation concluded it must complete three (3) longer-term animal studies (the “Long-Term Studies”) to confirm the dermal and systemic safety of Pennsaid®. The three Long-Term Studies are:

- a six (6) month repeat dose dermal toxicity study (the “Six-Month Tox Study”);
- a twelve (12) month repeat dose dermal toxicity study (the “Twelve-Month Tox Study”); and,
- a two (2) year dermal carcinogenicity study (the “Carc Study”) preceded by a dose finding trial (the “Carc Dosing Trial”).

The FDA confirmed in written minutes of a telephone meeting with the Corporation that the Carc Study can be completed post approval, provided no safety concerns are identified in

the Six-Month Tox Study or the Twelve Month Tox Study (together the "Tox Studies"). The Corporation has completed the Tox Studies and based upon its interpretation of the data believes there are no safety concerns such that, as per its agreement with the FDA, the Carc Study may be completed post approval. The Corporation completed the Carc Dosing Trial and in subsequent communication with the FDA during 2008 reached a Special Protocol Assessment Agreement on the Carc Study protocol design. This agreement provides the Corporation with the ability to commence the Carc Study. On February 4, 2009, the Corporation filed a complete response amendment to address all of the FDA's concerns raised in the Approvable Letter. Upon accepting the resubmission the FDA set August 5, 2009 as the date under the Prescription Drug User Fee Act (the PDUFA date), by which the FDA will advise Nuvo of its decision regarding Pennsaid®'s approvability; however, there is no guarantee that the FDA will complete its review in this timeframe. If approved by the FDA, Pennsaid® will be permitted to be sold and marketed in the United States. (See "Narrative Description of the Business – Topical and Transdermal Drug Delivery – Pennsaid®"). However, there can be no assurance, if or when, the FDA will approve the sale or marketing of Pennsaid® in the United States.

### ***Pennsaid® Plus***

The Corporation began exploring formulations to improve upon the original Pennsaid® formulation in late 2004. The Corporation has completed preliminary testing of a new, improved version of Pennsaid®, currently referred to as Pennsaid® Plus. While no clinical trials of this product have taken place to date, in vitro and in vivo tests have indicated that Pennsaid® Plus may increase the transport of diclofenac, the active therapeutic drug in both original Pennsaid® and Pennsaid® Plus, through the skin with less frequent dosing than Pennsaid® providing Pennsaid® Plus with potential advantages over Pennsaid® and with enhanced patent protection. The development of Pennsaid® Plus is an important step in the Corporation's plan to develop a family of topically applied drugs with applications in a number of therapeutic areas.

The Corporation has filed patent applications for improved versions of Pennsaid® including Pennsaid® Plus. (See "Narrative Description of the Business – Intellectual Property – Pennsaid® Plus").

Pennsaid® Plus is not currently approved for sale or marketing in any jurisdiction. The Corporation has had meetings with the FDA at which the FDA's information requirements for the approval of Pennsaid® Plus were discussed. Based on its most recent meeting with the FDA in 2008, the Corporation now intends to conduct two pivotal phase 3 clinical trials to demonstrate the clinical efficacy of Pennsaid® Plus. The Corporation will not commence the phase 3 clinical trials until certain goals are achieved including receipt of sufficient funds to complete the trials. Additional clinical and non-clinical studies may be required to support applications for the regulatory approval of Pennsaid® Plus in the U.S. and other jurisdictions in which the Corporation would wish to market the product. There can be no assurance that such trials will be sufficient for regulatory authorities or that studies will yield successful results or that the required regulatory approvals will be obtained. If approved for sale and marketing, the Corporation believes that Pennsaid® Plus will be more desirable than Pennsaid® as it is anticipated that less frequent dosing will offer improved patient compliance and ease of use while providing the same OA symptom relief as Pennsaid®.

Squire obtained an option to license Pennsaid® Plus in Canada as part of the January 16, 2006 transaction whereby Nuvo sold a portion of its Canadian Pennsaid® revenue stream to Squire. On December 21, 2006, Squire exercised its option to market and sell Pennsaid® Plus in Canada. On July 7, 2008, Squire acquired the rights to market Pennsaid® Plus in some

additional territories outside of North America where the Corporation does not currently have marketing partners for Pennsaid®, including South Africa and Israel. (See “— Pennsaid®” and “—Recent Financings and Corporate Transactions”).

### **Oxoferin™**

Oxoferin™, a topical wound healing agent, is a diluted form of WF10, a chlorite-based, immunomodulating drug. The Corporation believes that research to-date appears to indicate Oxoferin™ has a positive impact on wound healing leading to contraction, closure and faster healing of wounds.

Chronic, hard-to-heal wounds are a serious problem with an increasing incidence. Chronic wounds can be caused by such conditions as burns, pressure sores and poor circulation in the lower extremities. Co-morbid conditions, such as diabetes and atherosclerosis, reduce blood flow to the extremities and also increase the likelihood of developing chronic wounds such as diabetic foot ulcers and venous ulcers.

In 2002, there were an estimated six million chronic wound cases in the United States and the incidence of these wounds is increasing at approximately 10% per year. In 2004, some 71,000 people lost a foot or leg to complications from diabetes. Currently, it is estimated that the sales value of the advanced wound care market worldwide is approximately \$4 billion, and continues to grow at approximately 10 percent per year.

Oxoferin™ is marketed by Dimethaid GmbH and its partners in parts of Europe, Asia and South America as a topical wound healing agent under several trade names including Oxoferin™ and Oxovasin®. In 2008, the Corporation signed a distribution and license agreement with a regional pharmaceutical company for Russia and some of the former Soviet republics including the all of the Baltic States. The Corporation and its licensee are currently working to gain marketing authorizations in these territories, but do not expect to receive such authorizations until 2010 at the earliest. The Corporation’s patents associated with Oxoferin™ have expired and the Corporation is exploring improved formulations of this product. (See “Narrative Description of the Business — Intellectual Property”).

### **Recent Financings and Corporate Transactions**

In the past three years, the Corporation has raised approximately \$36.2 million in net proceeds from the issuance of Units (each Unit consisting of, a “Common Share” and a fraction of a warrant) and convertible debentures through both private placement agreements and public offerings. The Corporation has also raised approximately \$9.8 million from the exercise of warrants issued in connection with offerings of Common Shares, Units and Debentures over the same time period. The Corporation is continuing to explore further financing opportunities in order to commercialize Pennsaid® worldwide, develop other drugs in its product pipeline, and support general corporate purposes.

#### **2008**

On July 7, 2008, in connection with the agreement to amend and restate the Pennsaid® and Pennsaid® Plus licensing, supply and other arrangements in Canada, Squire invested \$2.0 million in the Corporation by way of a two-year convertible debenture (the “Squire 2008 Debenture”). This debenture bears interest at 8% per annum and is convertible into Nuvo Common Shares at a price of \$0.138 per share. Prior to conversion, the Squire 2008 Debenture is collateralized by revenue from Pennsaid® sales in Europe, a mortgage over

Nuvo's manufacturing facility in Québec, a charge on manufacturing assets and inventory in Québec and the Corporation's manufacturing intellectual property rights to the extent required to manufacture and market Pennsaid® in Canada. (See "Description of Capital Structure – Description of the Squire Debentures" and "– Products – Pennsaid®").

On May 29, 2008, the Corporation closed a private placement equity financing with Paladin (the "May 2008 Financing"). At closing, a total of 7,692,307 Common Shares of the Corporation were issued to Paladin at a price of \$0.13 per share for gross proceeds of \$1 million. In addition, the Corporation issued 769,230 common share purchase warrants of the Corporation (the "Paladin Warrants"), each whole warrant entitling the holder to acquire one common share at a price of \$0.169 per share until May 29, 2010. Once expenses associated with the financing were deducted, net cash proceeds were \$0.9 million. (See "Description of Capital Structure – Description of the Common Share Purchase Warrants Issued May 2008").

## 2007

On July 13, 2007, the Corporation closed a bought deal equity financing (the "July 2007 Bought Deal"). At closing, a total of 100 million units ("Units") were issued at a price of \$0.20 per Unit for gross proceeds of \$20 million. Each Unit consisted of one Common Share and one-half of a common share purchase warrant of the Corporation (each a "July 2007 Warrant"), each whole July 2007 Warrant entitling the holder to acquire one Common Share at a price of \$0.30 per Common Share until July 13, 2009. Once expenses associated with the financing were deducted, including an underwriting fee of 6%, net cash proceeds were \$18.5 million. The warrants, including July 2007 Warrants issuable in connection with the exercise of underwriter warrants issued to the underwriters for services provided in connection with the offering, were fair valued using the Black-Scholes option pricing model at \$4.8 million. Consequently, \$4.8 million of the cash proceeds are allocated to the warrants and the balance of \$13.7 million is allocated to the Common Shares. Each underwriter warrant is exercisable into one Unit at a price of \$0.20 per Unit until July 13, 2009. Under the terms of the Corporation's 2009 Warrant Incentive Program, the exercise price of the July 2007 Warrants has been reduced to \$0.125 until April 3, 2009. (See "– Warrant Incentive Programs" and "Description of Capital Structure – Description of the Common Share Purchase Warrants Issued July 2007").

## 2006

On June 20, 2006, the Corporation closed a bought deal equity financing of 37.5 million units (each, a "Unit") of the Corporation at a price of \$0.40 per Unit for gross proceeds of \$15 million (the "June 2006 Bought Deal"). Each Unit consists of one Common Share and one-third of one common share purchase warrant of the Corporation (each a "June 2006 Warrant"), each whole June 2006 Warrant entitling the holder thereof to acquire one Common Share at a price of \$0.50 per Common Share until June 20, 2009. Once expenses associated with the financing were deducted, including an underwriting fee of 5.75%, net cash proceeds were \$13.7 million. The June 2006 Warrants, including June 2006 Warrants issuable in connection with the exercise of the underwriter warrants issued to the underwriters for services provided in connection with the offering, were fair valued using the Black-Scholes option pricing model at \$2.2 million. Consequently, \$2.2 million of the cash proceeds were allocated to the June 2006 Warrants, and the balance of \$11.5 million was allocated to the Common Shares. Each underwriter warrant was exercisable into one Unit at a price of \$0.40 per Unit until June 20, 2008 at which time they expired. Under the terms of the Corporation's 2009 Warrant Incentive Program the exercise price of the June 2006 Warrants has been reduced to \$0.125 until April 3, 2009. (See "– Warrant Incentive Programs" and "Description of Capital Structure – Description of the Common Share Purchase Warrants Issued June 2006").

On January 16, 2006, the Corporation sold certain rights to receive Pennsaid® Canadian revenues to Squire, a wholly owned subsidiary of Paladin. As part of that transaction, the Corporation issued to Squire a \$500,000 convertible debenture bearing interest at 8% and repayable in 3 years. As per the terms of the debenture it was converted at the holder's request into Common Shares on the basis of \$0.456 per common share.

On December 21, 2006, Squire exercised its option to market and sell Pennsaid® Plus in Canada. Squire obtained this option in connection with the January 16, 2006 transaction. As part of that transaction, the Corporation issued to Squire a \$500,000 convertible debenture bearing interest at 8% and repayable in 3 years or on May 21, 2008 at the holder's option if, on that date, the Corporation had not commenced a pivotal phase 3 clinical trial for Pennsaid® Plus. The debenture was convertible into Common Shares on the basis of \$0.60 per common share. The Corporation did not achieve the specific milestone contained in the convertible debenture and Squire demanded repayment whereupon the Corporation repaid the debenture. (See "Description of Capital Structure – Description of the Squire Debentures" and "– Products – Pennsaid®").

#### Warrant Incentive Programs

On January 6, 2009, the Corporation announced that the Toronto Stock Exchange ("TSX") had approved a warrant incentive program (the "2009 Warrant Incentive Program") designed to encourage the early exercise of 3,901,898 June 2006 Warrants (the "June 2006 Warrants"), 50,000,000 July 2007 Warrants (the "July 2007 Warrants"), and 20,012,494 common share purchase warrants issued in connection with a financing completed in November 2004 (the "November 2004 Warrants"). The November 2004 Warrants could have been exercised at an exercise price of \$0.48 until November 16, 2009. (See "Description of Capital Structure — Description of the Common Share Purchase Warrants Issued November 2004").

In order to encourage the early exercise of the June 2006 Warrants, the July 2007 Warrants and the November 2004 Warrants, Nuvo amended the terms of such warrants so that upon payment of a reduced exercise price of \$0.125 (which represents the 5-day volume weighted average trading price of Common Shares as at the time the 2009 Warrant Incentive Program was announced) and surrender of the holder's warrant certificate in accordance with applicable procedures, the holder is entitled to receive one Common Share. The Corporation is providing the holders of the June 2006 Warrants, the July 2007 Warrants and the November 2004 Warrants an exercise period commencing on January 21, 2009 and ending on April 3, 2009. Any warrants that are not exercised under the 2009 Warrant Incentive Program will continue to be exercisable for Common Shares on the same terms as previously existed.

On November 20, 2006, the Corporation announced that the Toronto Stock Exchange ("TSX") had approved a warrant incentive program (the "2006 Warrant Incentive Program") designed to encourage the early exercise of 7,235,341 warrants issued in connection with a financing completed in June 2004 (the "June 2004 Warrants") (such warrants could have been exercised at an exercise price of \$0.73 until June 10, 2007), 30,461,940 November 2004 Warrants) (such warrants could have been exercised at an exercise price of \$0.45 until November 16, 2007 and are exercisable at \$0.48 between November 16, 2007 and November 16, 2009) and 12,499,995 June 2006 Warrants.

In order to encourage the early exercise of the June 2004 Warrants, the November 2004 Warrants and the June 2006 Warrants, Nuvo amended the terms of such warrants so that upon payment of a reduced exercise price of \$0.60, \$0.40 and \$0.40, respectively, and surrender of the holder's warrant certificate in accordance with applicable procedures, the holder was entitled

to receive one Common Share. The Corporation provided the holders of the June 2004 Warrants, the November 2004 Warrants and the June 2006 Warrants an exercise period commencing on December 11, 2006 and ending on January 31, 2007. During the exercise period, an aggregate of 19,548,455 warrants were exercised resulting in gross proceeds to the Corporation of approximately \$7.9 million. All warrants that were not exercised continued to be exercisable for Common Shares on the same terms as previously existed.

## **Dispositions**

On August 16, 2005, the Corporation raised \$7.5 million from the sale of DHCL to Paladin. On January 16, 2006, the Corporation received a further payment of \$3.25 million from Squire in consideration for additional rights to receive Pennsaid® Canadian revenues. On July 7, 2008, the Corporation received an additional \$2.5 million upon agreeing to amend and restate the Pennsaid® and Pennsaid® Plus arrangements in Canada (See “— Products – Pennsaid®” and “— Products – Pennsaid® Plus”).

In September 2005 and October 2005, the Corporation sold the principal assets of Dioptic, which distributed branded diagnostic and therapeutic ophthalmic products in Canada. The sale was completed in two separate transactions to two purchasers. Proceeds from the dispositions totalled \$550,000, of which \$175,000 was retained by one of the purchasers pending receipt by the purchaser of Ontario formulary coverage for certain product rights (represented by “DINs” or Drug Identification Numbers), failing which these rights would revert to the Corporation. The prescribed time period elapsed without the purchaser receiving approval; however, during 2006 the purchaser agreed to pay the Corporation \$50,000 of the retained funds to extend the prescribed time period. Subsequently, in the fourth quarter of 2006, the purchaser received formulary coverage and paid Nuvo the remaining retained funds of \$125,000.

On January 12, 2006, the Corporation sold its Markham, Ontario head office and furniture for \$2.7 million net of commissions and closing costs. On closing, US\$1.4 million (Cdn.\$1.6 million) was paid into escrow to discharge the mortgage on the property (as described below) and \$45,000 was retained by the purchaser to cover the Corporation’s leaseback of the office from closing to March 31, 2006. The resulting net cash proceeds to the Corporation were \$1.1 million.

The Corporation’s head office property was subject to an outstanding mortgage of US\$1.7 million (Cdn. \$2.0 million) including accrued interest. The balance due under this mortgage is in dispute with Leadenhall Bank & Trust Company Limited (“the mortgagee”), which is subject to court appointed liquidation in the Bahamas where it is situated. The dispute regarding the amount owing under the mortgage was the subject of an Ontario court action (the “Ontario Action”) that has since been dismissed by the courts for delay. In order to allow the sale of the Corporation’s former head office, the liquidator agreed to discharge the mortgage provided that US\$1.4 million of the sale proceeds be paid into escrow. (See “Narrative Description of the Business – Litigation, Regulatory Actions, Contingencies and Other Matters”).

On October 31, 2006, the Corporation entered into a binding agreement of purchase and sale with a third party for a property located in Varennes, Québec that was originally intended for a planned expansion of the Corporation’s manufacturing facility. Of the \$425,000 selling price, \$50,000 was paid on closing and the balance of \$375,000 was received in November 2007.

## **Acquisitions**

### ***Oxo Chemie AG***

In November 2004, the Corporation entered into an agreement with Dr. Kühne, the prior owner of Oxo Chemie, pursuant to which Dr. Kühne agreed to release the Corporation from its US\$27.7 million obligation to him incurred in respect of the Corporation's 2002 acquisition of Oxo Chemie, in return for the following consideration:

- \$4 million of units (each unit consisting of one Debenture and 1,667 November 2004 Warrants)
- 100% ownership of WF10 marketing rights for Thailand;
- a 40% ownership interest in Dimethaid AG, which owns intellectual property rights for WF10 (the Corporation retained the right to repurchase this ownership interest subject to certain conditions);
- 6% of all worldwide WF10 licensing fees and royalties earned by the Corporation; and
- a right of first offer to purchase, at a price specified by the Corporation, all or part of the worldwide WF10 intellectual property and exploitation rights in the event the Corporation chooses to sell such rights.

On May 31, 2005, the Corporation entered into more comprehensive agreements with Dr. Kühne to evidence these arrangements. At that time, the Corporation also transferred all shares of Dimethaid GmbH to Dimethaid AG, making Dimethaid GmbH a wholly owned subsidiary of Dimethaid AG. (See "Nuvo Research Inc. Structure – Corporate Structure – Dimethaid AG and Dimethaid GmbH").

### ***fqubed, Inc.***

In December 2005, the Corporation acquired all issued and outstanding shares of fqubed. fqubed, with the help of technology licensed from the University of California, has developed proprietary capabilities to identify innovative formulations that can efficiently deliver active therapeutics to and through the skin. Under the terms of the agreement, Nuvo issued 4,339,875 Common Shares in satisfaction of the US\$600,000 purchase price. Nuvo is also obligated to pay former fqubed shareholders a maximum US\$1.0 million in royalties for pharmaceutical products and a maximum US\$3.0 million for non-pharmaceutical products, based on sales of commercialized products that use specifically identified formulations developed by fqubed prior to the closing date. (See "Narrative Description of the Business — Technology — Topical and Transdermal Drug Delivery").

## **NARRATIVE DESCRIPTION OF THE BUSINESS**

Nuvo is a Canadian drug development company primarily focused on the research and development of drug products that are delivered to and through the skin. Nuvo is also involved in research and development activities involving WF10, a chlorite-based, immunomodulating drug through its 60% interest in Dimethaid AG. The Corporation refers to and manages these

activities as two distinct business and research segments: (i) topical and transdermal drug delivery; and (ii) immune system regulation.

### **Topical and Transdermal Drug Delivery**

The Corporation's Topical and Transdermal Drug Delivery platform is based upon the use of molecular skin penetration enhancers, transdermal carriers, to deliver drugs to and through the skin directly to the disease site. Unlike oral medications, Nuvo's topical products do not rely on bloodstream circulation to reach affected parts of the body; consequently they offer site-specific treatment while limiting systemic exposure to the active drug thereby reducing the potential for negative side effects, adverse events and potential drug-drug interactions.

Research studies conducted on behalf of the Corporation appear to confirm that using a transdermal carrier to deliver an effective pain relieving dose of diclofenac sodium results in significantly lower levels of diclofenac in the bloodstream, compared with published reports for diclofenac delivered orally.

Since acquiring fqubed in December 2005, the Corporation has increased its focus on identifying and developing a family of synergistic multiplexed molecular skin penetration enhancers ("MMPE™s"). The new molecular skin penetration enhancer systems will expand the Corporation's opportunities for developing drug products that can be delivered to and through the skin. (See "— Technology — Topical and Transdermal Drug Delivery").

The Corporation is actively conducting research on formulations utilizing these systems to build its drug candidate pipeline in pain and other therapeutic areas and has a number of formulations in research or in early stage pre-clinical development.

### ***Pennsaid®***

Pennsaid®, the Corporation's lead product, is used to treat the pain and symptoms associated with knee OA. OA is the most common joint disease affecting middle-age and older people. It is characterized by progressive damage to the joint cartilage and causes changes in the structures around the joint. These changes can include fluid accumulation, bony overgrowth, and loosening and weakness of muscles and tendons, all of which may limit movement and cause pain and swelling.

Pennsaid® combines a transdermal carrier DMSO with diclofenac sodium, a leading NSAID) and delivers the active drug through the skin directly to the site of pain. While, conventional oral NSAIDs expose patients to potentially serious systemic side effects such as gastrointestinal bleeding and cardiovascular risks, Nuvo's clinical trials suggest that some of these systemic side effects occur less frequently with topically applied Pennsaid®.

Based on data from national and regional surveys and applying these to 2005 U.S. Census data, the American College of Rheumatology ("ACR") reported that more than 21% of U.S. adults (46.4 million persons) were found to have self-reported doctor-diagnosed arthritis. This number is expected to increase by 40% to nearly 67 million over the next 25 years. In adults, arthritis is one of the leading causes of disability and is among the most common conditions resulting in work limitations. According to the Arthritis Foundation ("AF") most Americans are unaware of the seriousness of arthritis and the substantial negative impact it can have on an individual's quality of life and use of health-care resources. They estimate that it costs the U.S. economy more than \$128 billion annually. According to the AF, knee

osteoarthritis, the most frequent form of lower extremity arthritis, contributes to 418,000 knee replacement procedures annually and in 2006 accounted for \$19 billion in hospital charges.

A number of existing pharmaceutical products treat the pain associated with OA. The goal, according to the ACR, is “control of pain and improvement in function and health-related quality of life, with avoidance, if possible, of toxic effects of therapy”. The global osteoarthritis prescription drug market is estimated to have annual sales of approximately US\$4 billion. Of the many products in this market, most fall into one of the following categories:

- over-the-counter oral medications that are accessible without a doctor’s prescription, such as acetaminophen and low-dose NSAIDs such as ibuprofen and naproxen (Advil®, Motrin®, Aleve®);
- oral, full-dose, NSAIDs which are available by prescription only;
- topical NSAIDs, of which only one is approved by the FDA to treat the pain of OA and is available by prescription only;
- oral COX-2 selective NSAIDs which are available only by prescription; and
- oral narcotics, such as opioid analgesics which are available only by prescription.

Pennsaid® is a topical NSAID solution available only by prescription where approved. (See “General Development of the Business – Products – Pennsaid®”). In the multi-year development of Pennsaid® the Corporation has conducted multiple clinical studies that demonstrate both the safety and efficacy of Pennsaid® in the treatment of OA of the knee.

#### Study 106

A bioavailability study, known as “Study 106”, was conducted at the University of California, San Francisco (“UCSF”) in 1996, to determine in vivo the net effect of the enhanced skin penetration of Pennsaid®. The results of Study 106 indicated that Pennsaid® showed a distinctly different profile and yielded a much lower systemic absorption of diclofenac than oral diclofenac. Pennsaid®’s ability to rapidly penetrate the skin, while minimizing bloodstream uptake of diclofenac suggests that the active ingredient may remain within the tissue near the disease site for an extended period of time before it is metabolized or enters the bloodstream. Based on the absorption profile presented by Pennsaid®, researchers conducting the study had predicted a decrease in the risk of some side effects commonly linked to oral NSAIDs. This prediction was later confirmed in Phase 3 trials.

#### Study 107

A Phase 3 trial with patients suffering from knee OA, referred to as “Study 107” was conducted at seven sites in southern Ontario in 1996. The response to treatment was measured using the same standards applied to competing oral drugs: pain, stiffness, physical function and patient global assessment. Analysis showed that Pennsaid® provided statistically significant relief in all measures as compared to both a vehicle control group and those receiving a placebo solution. The safety results confirmed the prediction of reduced systemic toxicity, and detected only minor local skin irritation. The Corporation presented the study at the Osteoarthritis Research Society International’s 4th World Congress in September 1999 and at the 63rd Annual Scientific Meeting of the American College of Rheumatology in November 1999. This study has since been published in a Canadian peer-reviewed journal.

## Study 109 and Study 109US

Additional pivotal Phase 3 trials, referred to as Study 109 and 109US, conducted in 1999 and 2000 respectively confirmed that Pennsaid® relieves pains and improves physical function and patient global assessment. All patients in these studies suffered from moderate pain resulting from knee osteoarthritis. Again, no systemic toxicity was reported and the study was published in peer-reviewed journals.

## Study 110

A clinical study directly comparing Pennsaid® with oral diclofenac, in the maximum recommended daily dose, conducted in 2001 demonstrated that Pennsaid® is equivalent to oral diclofenac in relieving the symptoms of primary knee OA, while showing a lower incidence of gastrointestinal side effects. Equivalence was demonstrated in three primary outcome measures: pain, physical function, and patient global assessment. An oral presentation of these results was made at the 4th Annual European Congress of Rheumatology in June 2003. The study has since been published in the Journal of Rheumatology.

## Study 112 and Study 112E

In 2004, the Corporation launched two Phase 3 clinical studies designed with the input of the FDA to address concerns raised in the Non-Approvable Letter. The first study was to confirm efficacy, and to investigate the safety of the drug in combination with a conventional oral analgesic (oral diclofenac) (Study 112). The second study evaluated long-term safety (Study 112E).

Study 112 was completed in December 2005. The study enrolled 775 patients with primary OA of the knee. Patients in this five-armed, double-blinded, double-dummy, 12-week trial applied a topical solution and took an oral pill. The five arms of the study had patients receiving either: 1) Pennsaid® and an oral placebo; 2) a topical placebo and an oral placebo; 3) a topical vehicle-control (containing the same concentration of DMSO as in Pennsaid®) and an oral placebo; 4) a topical placebo and oral diclofenac or, 5) Pennsaid® and oral diclofenac. Pennsaid® (arm 1) was found to be superior to placebo (arm 2) with statistically significant improvement in all three primary outcome measures required by the FDA: pain relief ( $p=0.019$ ), improved physical function ( $p=0.046$ ) and improved patient overall health assessment (POHA) ( $p<0.0001$ ).

Additional results showed that Pennsaid® (arm 1) was superior to vehicle control (arm 3): pain,  $p=0.009$ ; physical function,  $p=0.026$ ; POHA,  $p=0.016$ . There was no statistical difference between vehicle control (arm 3) and placebo (arm 2), ( $p>0.05$  for all 3 variables) indicating that DMSO alone is ineffective for treating the symptoms of knee OA. There was no statistical difference between Pennsaid® (arm 1) and oral diclofenac (arm 4) for all three efficacy variables ( $p>0.05$ ). The side effect profile of Pennsaid® if combined with oral diclofenac (arm 5) was included in the trial at the FDA's request to evaluate whether there was any increased incidence of side effects beyond the expected additive profiles of Pennsaid® or oral diclofenac, used alone. The trial determined that there was no increased incidence beyond the additive profiles. This study was detailed in a poster presentation at the 2008 American College of Rheumatology Scientific Meeting in San Francisco.

The long-term open-label Phase 3 safety trial (Study 112E) was completed in the first quarter of 2006 and analysis of the data from Study 112E confirmed the safety profile of Pennsaid®.

Study 112E was a long-term multi-centre, single-arm safety study of Pennsaid® applied by patients with symptoms of OA of the knee. 793 patients in total were treated, 448 patients for at least 6 months and 116 patients for at least one year, satisfying the standard International Conference for Harmonization (ICH) long-term safety requirements. Over the course of the study, pre-defined safety parameters were prospectively monitored and patient reported adverse event information was collected at regularly scheduled visits. Parameters included patient history and routine physical examination, standard blood and urine tests and full ocular examination.

The results of this long-term safety trial confirm the safety profile of Pennsaid® evidenced in the previous 3-month safety/efficacy pivotal trials. The most prevalent adverse event noted was application site skin irritation in the form of dry skin - as has been observed in previous trials and is noted in both the Canadian and European product labels. However, the critical observation was that long-term use did not cause any new, unexpected adverse events.

### Regulatory Status

Pennsaid® has been approved for sale and marketing in a number of countries, including Canada, several Caribbean nations and a number of European countries including Greece, Italy and the United Kingdom. It has not received FDA approval allowing it to be sold and marketed in the United States.

The Corporation's initial submission for FDA approval to market Pennsaid® in the United States was made in 2001. In August 2002, in response to the Corporation's initial NDA application for Pennsaid®, the FDA sent the Corporation a non-approvable letter (the "Non-Approvable Letter"), detailing a number of deficiencies in the Corporation's application. In consultation with the FDA, the Corporation designed two new Phase 3 clinical trials, a 12-week efficacy trial and a long-term safety trial and conducted a pharmacokinetic study providing more information on DMSO in order to address the deficiencies cited by the FDA in the Non-Approvable Letter. The Corporation successfully completed all required trials and submitted an amended NDA to the FDA in June 2006.

On December 28, 2006, Nuvo received an Approvable Letter from the FDA for Pennsaid®. In the Approvable Letter, the FDA indicated that Pennsaid® is approvable subject to Nuvo satisfying certain conditions including the provision of additional nonclinical dermal safety and packaging data. None of the conditions in the Approvable Letter related to the clinical efficacy or the clinical safety of Pennsaid®. Furthermore, none of these conditions had been raised by the FDA in the Non-Approvable Letter of August 2002. The FDA has not requested that Nuvo conduct any additional Phase 3 clinical trials as a condition of approval.

During 2007, the Corporation engaged in communications with the FDA in an effort to clarify the Agency's expectations as outlined in the Approvable Letter. Through these communications the FDA clarified certain of its requirements for additional information relating to Pennsaid®. Based on the contents of the Approvable Letter and these clarifications, the Corporation completed several Short-Term Studies. In addition, the Corporation concluded it must complete three (3) Long-Term Studies to confirm the dermal and systemic safety of Pennsaid®. The three Long-Term Studies are:

- a six (6) month repeat dose dermal toxicity study (the "Six-Month Tox Study");
- a twelve (12) month repeat dose dermal toxicity study (the "Twelve-Month Tox Study");
- and,

- a two (2) year dermal carcinogenicity study (the “Carc Study”) preceded by a dose finding trial (the “Carc Dosing Trial”).

The FDA confirmed in written minutes of a telephone meeting with the Corporation that the Carc Study can be completed post approval, provided no safety concerns are identified in the Six Month Tox Study or the Twelve Month Tox Study (together the “Tox Studies”). The Corporation has completed the Tox Studies and based upon its interpretation of the data believes there are no safety concerns such that, as per its agreement with the FDA, the Carc Study may be completed post approval. The Corporation completed the Carc Dosing Trial and in subsequent communication with the FDA during 2008 reached a Special Protocol Assessment Agreement on the Carc Study protocol design. This agreement provides the Corporation with the ability commence the Carc Study. On February 4, 2009, the Corporation filed a complete response amendment to address all of the FDA’s concerns raised in the Approvable Letter. Upon accepting the resubmission the FDA set August 5, 2009 as the date under the Prescription Drug User Fee Act (the PDUFA date), by which the FDA will advise Nuvo of its decision regarding Pennsaid®’s approvability; however, there is no guarantee that the FDA will complete its review in this timeframe. If approved by the FDA, Pennsaid® will be permitted to be sold and marketed in the United States. (See “Narrative Description of the Business – Topical and Transdermal Drug Delivery – Pennsaid®”). However, there can be no assurance, if or when, the FDA will approve the sale or marketing of Pennsaid® in the United States.

### ***Pennsaid® Plus***

The Corporation began exploring formulations to improve upon the original Pennsaid® formulation in late 2004. The Corporation has completed preliminary testing of a new, improved version of Pennsaid®, currently referred to as Pennsaid® Plus. While no clinical trials of this product have taken place to date, in vitro and in vivo testing have indicated that Pennsaid® Plus may increase the transport of diclofenac, the active therapeutic drug in both original Pennsaid® and Pennsaid® Plus, through the skin with less frequent dosing than Pennsaid®. The development of Pennsaid® Plus is an important step in the Corporation’s plan to develop a family of topically applied drugs with applications in a number of therapeutic areas.

The Corporation has filed patent applications for improved versions of Pennsaid® including Pennsaid® Plus. (See “Narrative Description of the Business – Intellectual Property – Pennsaid® Plus”).

Pennsaid® Plus is not currently approved for sale or marketing in any jurisdiction. The Corporation has had meetings with the FDA at which the FDA’s information requirements for the approval of Pennsaid® Plus were discussed. Based on its most recent meeting with the FDA in 2008 the Corporation now intends to conduct two pivotal phase 3 clinical trials to demonstrate the clinical efficacy of Pennsaid® Plus. The Corporation will not commence the phase 3 clinical trials until certain goals are achieved including receipt of sufficient funds to complete the trials. Additional clinical and non-clinical studies may be required to support applications for the regulatory approval of Pennsaid® Plus in the U.S. and other jurisdictions in which the Corporation would wish to market the product. There can be no assurance that such trials will be sufficient for regulatory authorities or that studies will yield successful results or that the required regulatory approvals will be obtained. If approved for sale and marketing, the Corporation believes that Pennsaid® Plus will be more desirable than Pennsaid® as it is anticipated that less frequent dosing will offer improved patient compliance and ease of use while providing the same OA symptom relief as Pennsaid®.

Squire obtained an option to license Pennsaid® Plus in Canada as part of the January 16, 2006 transaction whereby Nuvo sold a portion of its Canadian Pennsaid® revenue stream to Squire. On December 21, 2006, Squire exercised its option to market and sell Pennsaid® Plus in Canada. On July 7, 2008, Squire acquired the rights to market Pennsaid® Plus in some additional territories outside of North America where the Corporation does not currently have marketing partners for Pennsaid®, including South Africa and Israel. (See “— Pennsaid®” and “—Recent Financings and Corporate Transactions”).

### ***Early Stage Drug Development***

The Corporation is actively conducting research on formulations utilizing its molecular skin penetration enhancer systems to build its topical and transdermal drug candidate pipeline. The Corporation is focusing its research in the areas of pain and selected indications in the field of dermatology. A number of formulations are under research or in early stage pre-clinical development.

#### Pain

In addition to Pennsaid® and Pennsaid® Plus Nuvo is developing topical pain medications for a variety of pain conditions, including acute and chronic pain of inflammatory, nociceptive and neuropathic origin. All of these pain medications will be designed to treat the pain locally while limiting systemic exposure to the active drug thereby reducing the potential for negative side effects, adverse events and potential drug-drug interactions. The drug product candidates under development are at various stages of formulation and pre-clinical development. Development of these topical drug candidates is being aided by fqubed's screening technology. (See “— Technology – Topical and Transdermal Drug Delivery”).

#### Dermatology

The Corporation is also pursuing development of drugs to treat dermatological indications. Nuvo's research in this area has been directed towards pre-clinical activities on a topical antifungal drug candidate intended for use in treating onychomycosis (a nail fungal infection that resides in both the nail and nail bed). Onychomycosis is responsible for approximately half of all nail disease and affects an estimated 15% to 20% of people over age 40 in North America and the incidence of onychomycosis continues to increase as aging populations are more vulnerable to the disease. Existing oral treatments have the risk of significant and serious side effects such as liver, kidney and other organ toxicities and tend to be ineffective as the recurrence rate of the infection is high. Existing topical medications often cannot penetrate the nail well enough to provide a cure as the fungus infects both the nail and the tissue under the nail. The Corporation believes that there is a large unmet need for a topical drug product which offers increased efficacy over existing topical drugs and reduces the risk of adverse events associated with oral medications.

### **Immune System Regulation**

The immune system provides an essential defence to micro organisms, cancer and substances it sees as foreign and potentially harmful. The Corporation's Immune System Regulation platform, WF10, a solution of OXO-K993 containing stabilized chlorite ions, focuses on supporting the immune system by targeting the macrophage, a type of white blood cell that coordinates much of the immune system, to regulate normal immune function. All immune

system regulation research is carried out through Dimethaid AG in which the Corporation has a 60% interest.

### **WF10**

WF10, a solution of OXO-K993 containing stabilized chlorite ions, appears to act on the macrophage. Normally functioning macrophages can alternate between one of two basic states: phagocytic and inflammatory. Phagocytic macrophages digest invading organisms, such as viruses, and initiate a biological defence pathway. Inflammatory macrophages, in turn, induce a variety of reactions, including fever, sweating, swollen glands, malaise and appetite loss, the common, uncomfortable signs of illness. Such responses, while entirely normal, must be turned on and off in a controlled manner. If left unchecked pathogens can overdrive the system toward the inflammatory state creating an imbalance that may lead to such medical disorders as chronic inflammation, immune deficiency, organ damage and tumour proliferation.

WF10's proposed mode of activity is based on a theory about how macrophages regulate the immune system. Research suggests that, in some cases, WF10 may rebalance improperly functioning immune systems. The drug has potential applications in adjuvant cancer therapy, diseases related to immune deficiencies, and the management of chronic viral infections.

In 1999, McGrath and Kodelja published a paper in an industry publication entitled: "Balanced Macrophage Activation Hypothesis: A Biological Model for Development of Drugs Targeted at Macrophage Functional States". This essay suggests that WF10 encourages a switch in macrophage state from inflammatory to phagocytic, or vice versa, rebalancing the system and restoring proper immune function.

During the initial development of WF10, it was hypothesized that, because of its predicted effects on the immune system, WF10 might be successfully utilized as part of the treatment of HIV/AIDS patients. In July 2004, the Corporation completed initial analysis of data from Oxo Chemie's Phase 3 AIDS study showing that WF10 failed to achieve the anticipated results. The study, conducted in 229 late-stage HIV/AIDS patients at 32 sites across the U.S. and Canada, indicated no statistical difference between WF10 and placebo in the time to onset of clinical progression, defined as any new AIDS-defining event or death ( $p=0.8558$ ). Consequently, the Corporation is no longer exploring the treatment of HIV/AIDS as a potential use of WF10.

Notwithstanding the disappointing results of the HIV/AIDS trial, management believes that WF10 has potential in the treatment of other conditions. The Corporation has received encouraging results from independent researchers who have used WF10 or conducted informal pilot trials in patients with cancer and other medical conditions.

On August 24, 2005, the Corporation announced a new Phase 2 trial using WF10 as an adjuvant treatment for inoperable pancreatic cancer. The study commenced in February 2006 and is being conducted in Germany at the University of Heidelberg and the National Centre for Tumor Diseases, under the supervision of coordinating investigator Prof. Dr. Angela Märten. Enrollment was planned to include up to 43 patients with advanced, inoperable cancer who would receive oral capecitabine (Xeloda®), a chemotherapeutic drug currently used in cancer treatment, with WF10 co-therapy.

Cancer of the pancreas is the fourth leading cause of cancer death in the United States and over 37,000 new cases are expected to be diagnosed in 2008 and The Canadian Cancer

Society estimates over 3,750 deaths from this malignancy in 2008. Over 200,000 new cases of pancreatic cancer are diagnosed throughout the world every year with the incidence higher in western countries. Metastatic cancer of the pancreas is one of the deadliest forms of cancer as patients have a five-year survival rate of less than 5% and an average life expectancy of four to six months.

In late 2008, the Corporation had enrolled sufficient patients to conduct the interim analysis included in the study protocol. Preliminary results of the interim analysis indicate that the primary end point, greater than six months survival, was successfully achieved. However, it is unclear, based on the open-label study design and the data reviewed whether the positive results could be confirmed in a placebo controlled study. The researchers and scientists involved in the study believe that obtaining additional positive data from the continuation of the current study would not aid in this assessment. As a consequence, the Corporation ceased study enrolment and notified Germany's Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte) ("BfArM"), the German regulatory authority that oversees all clinical trials, of its decision to terminate the study in December 2008. The Corporation will continue to analyze the interim study results, including a more detailed analysis of the Quality of Life ("QoL") data collected during the study. In addition, discussions between the Corporation and both the University of Heidelberg and the National Centre for Tumor Diseases are ongoing as the data is analyzed and the best path forward determined.

Current concepts in cancer biology suggest that the inflammatory environment in the pancreas may enhance signalling pathways of tumour growth factors and other chemokines. Previous work has suggested that treatment with WF10 may modulate the immune response by influencing the monocyte/macrophage system, natural killer cells and cytotoxic T-lymphocytes. This activity may exert an adjuvant anti-tumour effect resulting in increased survival and improved quality of life for patients with pancreatic cancer.

A number of additional studies would need to be conducted before the Corporation is in a position to submit WF10 for regulatory approval for the treatment of pancreatic cancer or any other illness and there can be no assurance that the results of these studies would be favourable or that regulators would approve WF10 for these or other purposes. Any such studies and approvals would be expected to take a number of years. (See "General Development of the Business – Products – Oxoferin™").

WF10 is approved in Thailand as a treatment for post radiation cystitis, but is not otherwise approved for marketing and sale elsewhere except in its diluted form, Oxoferin™ (See "— Oxoferin™"). The Corporation does not hold patents on WF10 or for every potential use of WF10; however, it does hold patents and has filed patent applications for the use of WF10 for certain prescribed purposes in some jurisdictions. (See "— Intellectual Property").

### **Oxoferin™**

Chronic, hard-to-heal wounds are a serious problem with an increasing incidence. Chronic wounds can be caused by such conditions as pressure sores and poor circulation in the lower extremities. Co-morbid conditions, such as diabetes and atherosclerosis, reduce blood flow to the extremities and also increase the likelihood of developing chronic wounds.

In 2002, there were an estimated six million chronic wounds cases in the United States and the incidence of these wounds is increasing at approximately 10% per year. In 2004, some 71,000 people lost a foot or leg to complications from diabetes. Currently, it is estimated that the

sales value of the advanced wound care market worldwide is approximately \$4 billion, and continues to grow at approximately 10 percent per year.

A diluted form of WF10 is marketed by the Corporation's European subsidiary in parts of Europe, Asia and South America as a topical wound healing agent under several trade names including Oxoferin™. The Corporation believes the research to-date appears to indicate that, Oxoferin™ has a positive impact on wound healing leading to contraction, closure and faster healing of wounds. The Corporation's patents associated with Oxoferin™ have expired and the Corporation is exploring improved formulations of this product. (See "— Intellectual Property").

### Revenue breakdown

For the year ended December 31, 2008, Pennsaid® accounted for 87% of Nuvo's total revenue versus 86% in the year ended December 31, 2007.

<u>Revenue by geographical area (\$ thousands)</u>	<u>Year ended December 31, 2008</u>	<u>Year ended December 31, 2007</u>
Canada	4,009	\$2,457
Europe	5,698	\$3,820
Other	1,020	\$ 901

The increase in European revenue was driven by a full year of marketing Pennsaid® in Greece by the Corporation's distributor Vianex S.A. ("Vianex") following its launch in the first half of 2007. In Greece, Pennsaid® has full formulary coverage which makes it more accessible to the majority of the Greek population suffering from OA.

### Sales and Marketing

The Corporation's drug products are required to have received applicable regulatory approvals prior to their marketing and sale. Once such required regulatory approval is received, the Corporation typically enters into arrangements with third parties for the marketing and sale of the approved products in order that it can remain focused on the development of additional drugs.

#### ***Pennsaid®***

##### *Canada*

A Notice of Compliance was issued by Health Canada in March 2003, and Pennsaid® was officially launched in Canada in April 2003 as a prescription treatment for knee osteoarthritis symptoms. Initially, the Corporation used its own sales force to market Pennsaid® to Canadian health-care professionals.

The Corporation's former subsidiary, DHCL, owned the rights to distribute Pennsaid® in Canada. In February 2004, DHCL entered into a 10-year co-promotion agreement, effective March 1, 2004, with Solvay Pharma Inc. ("Solvay") an international pharmaceutical company. Under the agreement, Solvay and DHCL provided joint sales and marketing support in Canada. In return, Solvay received a portion of Canadian Pennsaid® revenues. The agreement provided for each party to regularly re-evaluate performance, sales territory alignments and promotional spending.

On January 4, 2005, DHCL and Solvay entered into an amended agreement covering Canadian marketing and sales of Pennsaid® effective as of that date (“Revised Co-Pro Agreement”). Under the Revised Co-Pro Agreement, Solvay assumed primary responsibility for Pennsaid® sales and promotion in Canada.

On August 16, 2005, the Corporation sold DHCL to Paladin for upfront payments totalling \$7.5 million, plus a long-term agreement calling for Nuvo to continue supplying Pennsaid® for the Canadian market. The agreement also provided that the Corporation would continue to share in certain future operating revenues arising from Canadian Pennsaid® sales in excess of target amounts until 2014. On January 16, 2006, rights to certain residual Canadian Pennsaid® sales revenues previously held by Solvay under the Revised Co-Pro Agreement reverted to the Corporation and were transferred to Squire, which was then a wholly owned subsidiary of Paladin, in consideration of an upfront \$3.25-million payment, an additional share of future operating profits and future royalties on the sales of Pennsaid® commencing in 2010. Additionally, the Corporation provided certain guarantees relating to the market performance of Pennsaid® in the Canadian market over a four year period which could have required payments to be made by the Corporation if performance targets were not met. Upon closing of this transaction, Squire held 100% of the marketing rights for Pennsaid® in Canada.

On July 7, 2008, the Corporation and Squire reached an agreement to amend and restate the Pennsaid® and Pennsaid® Plus licensing, supply and other arrangements in exchange for payments totalling \$2.5 million by Squire to the Corporation, including \$0.6 million in full settlement of amounts receivable relating to Ontario Innovation Tax Credits, \$0.9 million to settle obligations under the original licensing arrangements and \$1.0 million as a prepayment of future royalties that would otherwise be payable by Paladin to the Corporation through December 31, 2010 (the “Amended and Restated Canadian Licensing Arrangements”). Under the terms of the Amended and Restated Canadian Licensing Arrangements the Term was increased to 99 years and now ends in August 2104. As part of the new arrangements, the Corporation relinquished the right to share in certain future operating revenues in excess of target amounts. However, effective January 1, 2011 and until the end of the Term, Squire will pay the Corporation a royalty based upon Canadian sales of Pennsaid®.

As a result of these arrangements, since August 16, 2005, the Corporation’s revenues have not included sales revenue from the sale of Pennsaid® in Canada for retail distribution, but have included contract manufacturing revenue from the manufacture and supply of Pennsaid® to Squire, a share of Canadian revenues above specified targets under the original agreements and systematically amortized portions of the upfront payments made by Squire to the Corporation. Commencing January 2011, the Corporation’s revenues will also include a royalty based on Canadian sales of Pennsaid®. (See “General Development of the Business – Products - Pennsaid®” and “—Dispositions”).

#### *United States*

Pennsaid® is not currently approved for sale or marketing in the United States. The Corporation expects that sales and marketing of Pennsaid® would commence in the United States as soon as practicable after receiving FDA approval. However, there can be no assurance that such approval will be forthcoming.

Nuvo does not currently have the resources to market and sell Pennsaid® in the United States without assistance from a licensee or partner with U.S. sales and marketing capabilities. Over the past three years the Corporation, with the assistance of outside consultants, identified

several suitable partners for the United States. The Corporation continues to discuss the sale and marketing of Pennsaid® in the U.S. with potential licensees and partners.

#### *United Kingdom*

In the United Kingdom, the Medicines Control Agency granted the Corporation final marketing approval (“MA”) for Pennsaid® in November 2000, and the product was officially launched in March 2001. In June 2002, the Corporation’s then subsidiary, International terminated an agreement giving Provalis Healthcare Limited (“Provalis”) exclusive Pennsaid® distribution rights in the U.K. after Provalis failed to purchase contracted minimum quantities. Provalis initiated arbitration proceedings in December 2002, challenging Dimethaid International’s right to terminate, and on December 16, 2003, the U.K. arbitrator awarded Provalis GBP 1.6 million (CDN \$3.5 million). This amount was settled in 2005 with a payment less than the full amount of the arbitration judgment.

After terminating the Provalis distribution agreement, Dimethaid International entered into a new agreement with In2Focus Sales Development Services Limited (“In2Focus”), a contract sales organization, to promote Pennsaid® in the U.K. The Corporation subsequently terminated this contract in September 2004 as the revenue generated was significantly less than the costs incurred. In2Focus asserted a claim for damages against the Corporation on the basis that the Corporation was not entitled to terminate the contract. The amount claimed by In2Focus was settled in 2005 with a payment of less than the full amount claimed.

Pennsaid® continues to be distributed in the U.K. through Movianto UK Limited (formerly Healthcare Logistics Limited), the U.K.’s largest healthcare logistics specialist; however, there is currently no active Pennsaid® promotion.

#### *Other European Countries*

On the basis of the U.K. approval, the Corporation applied for additional Pennsaid® approvals in the European Union (“E.U.”) through the Mutual Recognition Procedure (“MRP”). Under this process, the U.K. acts as the Corporation’s Reference Member State (“RMS”) and requests that all Concerned Member States in the European Union recognize the MA granted in the U.K. as the RMS. In the European Economic Area, a medicinal product may only be placed on the market when an MA has been issued by a competent authority. Pursuant to the Corporation’s first application, it received MRP approval and MAs were issued by competent authorities in Austria, Finland, Italy and Luxembourg. Subsequent to receiving these MAs the Corporation formed marketing and distribution agreements with Tramedico International B.V. for the Benelux countries of Belgium, the Netherlands and Luxembourg (although they never launched the product in any of these markets) and Italchimichi S.p.A, a European Rx-Alliance member, for Italy where Pennsaid® was launched in mid-2003.

To address other markets within the E.U. and the European Free Trade Association (“EFTA”), the Corporation restarted the Pennsaid® MRP in September 2002, and in the second half of 2003, received additional MRP approvals and MAs in Greece, Iceland, and Portugal. In January 2004, the Corporation entered into an agreement with former Rx-Alliance member, Jaba Farmacêutica S.A. (“Jaba”), (subsequently renamed Jaba Recordati S.A.) to distribute Pennsaid® throughout Portugal, Madeira and the Azores. In January 2005, Jaba officially launched Pennsaid® in Portugal, but subsequently stopped promoting the product in this market and as a result, in December 2007, the Corporation terminated this agreement. In February 2004, the Corporation entered into an agreement with Vianex, also an Rx-Alliance member, for

the exclusive distribution of Pennsaid® in Greece. In the second quarter of 2007, Vianex launched Pennsaid® in Greece and continues to actively market the product.

Nuvo does not have the resources to market and sell Pennsaid® in any Eastern or Western European countries without assistance from a licensee, distributor or partner with sales and marketing capabilities and local regulatory knowledge. Over the past year, the Corporation, with the assistance of outside consultants, has continued to explore regulatory pathways to approval in European countries in which it has not yet received approval and has continued to identify potential partners in European countries in which Pennsaid® is approved, but not currently licensed. The Corporation continues to discuss the potential sale and marketing of Pennsaid® in these markets with potential licensees and partners, but has decided not to seek new MAs in additional E.U. nations until it has completed its resubmission to the FDA.

### *Caribbean*

Pennsaid® is commercially available in certain Caribbean countries where marketing authorization comes automatically with regulatory approval in the United Kingdom and Canada. The Corporation had a distribution agreement with A.S. Bryden & Sons (Barbados) Ltd. (“Bryden”) covering most Caribbean countries including Anguilla, Antigua, Barbados, Grenada, Montserrat, St. Kitts & Nevis, St. Lucia, St. Vincent and the British Virgin Islands. In Jamaica, where local approval is required, the Corporation received authorization to market Pennsaid® in February 2004, but has not yet launched the product. Bryden did not achieve the minimum annual sales targets in its distribution agreement with the Corporation and had not placed an order for Pennsaid® in several years. As a result, the Corporation terminated the agreement with Bryden in 2008.

### ***Pennsaid® Plus***

Pennsaid® Plus has not been approved for sale or marketing in any jurisdiction. On December 22, 2006, Squire exercised its right to enter into a license with Nuvo to sell and market Pennsaid® Plus in Canada. Squire obtained an option to license Pennsaid® Plus as part of the January 16, 2006 transaction whereby Nuvo sold a portion of its Canadian Pennsaid® revenue stream to Squire. On July 7, 2008, Squire acquired the rights to market Pennsaid® Plus in some additional territories outside of North America where the Corporation does not currently have marketing partners for Pennsaid®, including South Africa and Israel. (See “General Development of the Business – Products – Pennsaid®” and “—Pennsaid® Plus” and “—Dispositions”).

### ***WF10***

WF10 is approved in Thailand as a treatment for post radiation cystitis. WF10 has not been approved for sale or marketing in any other jurisdiction.

### ***Oxoferin™***

In Europe, marketing authorizations for Oxoferin™ were received for Austria, Hungary, Germany, Switzerland and Portugal between 1985 and 1995. Of these European countries, Oxoferin™ is currently sold in Germany under the trade name “Oxovasin®”. Oxoferin™ also gained marketing authorizations in several countries in Asia and South America during the same time period. Oxoferin™ is currently authorized for sale and marketed in India, Indonesia, Pakistan, Thailand and Venezuela. The Corporation sells the product to its customers in these markets in two forms depending on the terms of the respective marketing arrangements. In

certain markets the Corporation sells Oxoferin™ pre-packaged to local distributors. In the remaining markets, the raw material, OXO-K993,, is sold to the customer who then produces Oxoferin™ for the local market. In 2008, the Corporation signed a distribution and license agreement with a regional pharmaceutical company for Russia and some of the former Soviet republics including all of the Baltic States. The Corporation and its licensee are currently working to gain marketing authorizations in these territories, but do not expect to receive such authorizations until 2010 at the earliest.

## **Manufacturing and Facilities**

Nuvo's long-term business strategy does not include manufacturing, and management expects to rely on partners or contracted third parties for the production of drug products developed in the future. However, as the Corporation already has production facilities for its current commercial drug, Pennsaid®, management has decided to continue operating its own manufacturing facility for the foreseeable future.

In February 2000, the Corporation acquired its existing manufacturing facility in Varennes, Québec, with manufacturing, bottling and packaging capabilities and a research laboratory. In June 2000, the Corporation received an Establishment License from Health Canada in recognition of compliance with Good Manufacturing Practices ("GMP") regulations. In November 2000, after another successful GMP inspection, the U.K. Medicines Control Agency approved the facility for the manufacture, testing and warehousing of drug products destined for member countries in the E.U.. In February 2002, the plant passed an FDA pre-approval manufacturing inspection as part of the U.S. Pennsaid® NDA review. In December 2006, the plant was notified that it had passed an FDA inspection conducted by the Department of Health and Human Services in October 2006 as part of the Pennsaid® amended NDA review. The facility remains in compliance with current GMP regulations and is the production site for commercial quantities of Pennsaid® worldwide.

The facility is expected to continue operating below full capacity unless and until the FDA approves Pennsaid® and marketing begins in the United States. To maximize capacity utilization in the past, the Corporation had pursued contract manufacturing opportunities. While these activities did not affect the ability to supply Pennsaid®, the Corporation decided in mid-2006 to suspend the pursuit of these opportunities so the facility could focus its efforts on preparing for FDA approval of the site, the potential US launch of Pennsaid® and clinical batch production for Pennsaid® Plus. Given the delay in Pennsaid®'s FDA approval the Corporation pursued select contract manufacturing opportunities to utilize excess capacity in 2008. The Corporation expects that, with the installation of additional production equipment, the majority of which is readily available, its current manufacturing facilities have the production capacity to meet current and anticipated demand for Pennsaid®.

The Corporation also owns a 3,000-square-foot manufacturing facility in Wanzleben, Germany, acquired in May 2002 as part of the Oxo Chemie acquisition. This plant produces OXO-K993, the active ingredient in WF10 and Oxoferin™. (See "General Development of the Business – Acquisitions – Oxo Chemie AG").

On October 31, 2006, the Corporation entered into a binding agreement of purchase and sale with a third party for the sale of a partially constructed, unoccupied facility adjacent to the existing manufacturing facility in Varennes, Québec. The Corporation determined that the partially constructed facility was not required to meet the Corporation's present or planned manufacturing requirements. (See "General Development of the Business – Dispositions").

## **Intellectual Property**

### ***Pennsaid®***

The Canadian and U.S. Pennsaid® patents have expired. However, if FDA approval of Pennsaid® is granted in the United States, the Corporation has applied for and expects to receive a three-year period of marketing exclusivity from the date of approval pursuant to a 1984 United States federal law, the Drug Price Competition and Patent Term Restoration Act, informally known as the "Hatch-Waxman Act", and Code of Federal Regulations ("C.F.R.") 314.108(b)(4) which provide that a product filed as a 505(b)(2) application and supported by sponsor initiated clinical studies required as a condition of approval is entitled to three years of marketing exclusivity starting from the effective date of approval. This period of marketing exclusivity would prohibit the approval of generic versions of Pennsaid® in the United States for three years from the effective date of approval.

The European Pennsaid® patent (covering Austria, Belgium, France, Germany, Italy, Liechtenstein, Luxembourg, Netherlands, Sweden, Switzerland and the United Kingdom) expired in June 2006. In Italy the Corporation has a Supplementary Protection Certificate that extends the life of this patent until March 2011. (See "Risk Factors – Patents and Proprietary Technology")

### ***Pennsaid® Plus***

The Corporation has filed patent applications for Pennsaid® Plus and other related formulations.

### ***Other Early Stage Drug Development - Pain***

On May 29, 2008, the Corporation announced that it licensed the exclusive rights from Paladin to develop and commercialize a novel topical pain formulation with the potential to treat inflammatory and neuropathic pain conditions. The formulation is in the formulation optimization stage and is the subject of a pending patent application.

Nuvo issued 961,538 common shares to Paladin having a value of \$125,000 for the right to commercialize this topical pain product. As part of the transaction, Paladin may receive an additional payment of \$250,000 upon achievement of a regulatory milestone and will have rights to market, distribute and sell the product in Canada, South America, Central America and South Africa. Nuvo will receive royalties on Paladin sales and will have exclusive rights to exploit the licensed formulation in all other territories, including the United States.

A provisional patent application covering other topical pain formulations was filed in 2008. These formulations are in pre-clinical development.

### ***Topical Antifungal***

The Corporation has a pending U.S. patent application covering certain topical nail formulations to treat onychomycosis.

### ***Multiplexed Molecular Penetration Enhancer ("MMPE™") Technology***

Patent applications claiming certain combinations of particular molecular penetration enhancers ("MPE™s") together with certain active drugs in topical formulations have been filed.

### ***High Throughput Experimentation (“HTE”) Technology***

To protect its HTE equipment, technology and methods, the Corporation treats relevant information as trade secrets that are not made available or accessible to the public. Some other aspects of the HTE technology are protected by pending patents that have been filed by the Corporation or licensed by the Corporation from the University of California.

### ***WF10***

With the acquisition of Oxo Chemie on May 31, 2002, the Corporation acquired patents relating to the immune regulation technology underlying WF10 some of which have since expired. The Corporation does not hold composition of matter patents on WF10 itself or on all its potential uses, but does hold patents and has filed patent applications for particular prescribed uses of WF10.

### ***Oxoferin™***

All Oxoferin™ composition of matter patents have expired. The Corporation is conducting research with a view to developing an improved version of Oxoferin™ with enhanced wound healing abilities. Those research efforts may lead to new patent applications.

### ***Confidential Information and Trade Secrets***

In addition to patent protection, the confidential nature of the Corporation’s expertise and its trade secrets provides a period of exclusivity with respect to processes or products developed by, or for, the Corporation and its exclusive benefit. The Corporation believes it has taken steps reasonably necessary to protect the confidentiality of its commercially sensitive activities.

### ***Technology***

#### ***Topical and Transdermal Drug Delivery***

Nuvo believes it is uniquely positioned to research and develop new drug product candidates for delivery to and through the skin. First, Nuvo has developed several penetration enhancer formulations, MMPE™(s), that interact with the skin so as to modify its permeability thereby allowing certain drug molecules to pass into and through the skin to proximate tissues. Second, Nuvo operates HTE systems that allow its scientists to rapidly screen combinations of existing molecular penetration enhancers MPE™s and large numbers of potential drug formulations to measure their ability to permeabilize and permeate the skin. Third, the Corporation has assembled a team of scientists who have and continue to develop expertise in topical and transdermal drug delivery.

Nuvo’s topical and transdermal drug product focus is primarily on the treatment of pain, particularly in cases where changing the dosage form of proven active drugs from oral to topical provides the possibility of clinical benefit, with reduced systemic exposure and fewer systemic side effects. The Corporation is also using its technology to pursue drugs to treat dermatological indications. The Corporation’s HTE platforms also have practical utility for diverse use in pharmaceutical, cosmetic, personal care, diagnostic and medical device applications, where formulations suitable for modulating one or more properties of the skin, such as permeability, need to be developed. The Corporation intends to continue collaborations with third parties, directed towards either developing prospective products outside of its focus on

pain and dermatology or advancing its HTE capabilities. In 2008, the Corporation signed a research and development collaboration agreement with a Fortune Global 500 company. Under the collaboration agreement, fqubed will expand the scope of its TEMPEST™ HTE platform to evaluate potential formulations for its partner's product portfolio.

#### Multiplexed Molecular Penetration Enhancer ("MMPE™") Technology

Nuvo's pipeline of prospective drug candidates for delivery to or through the skin leverages its MMPE™ technology. The outermost layer of the skin, the stratum corneum, functions as an extremely effective barrier. The stratum corneum is comprised of many different types of molecules. Certain molecules, which Nuvo calls MPE™s, can interact with molecules in the stratum corneum to enhance its permeability. Nuvo believes that an effective way to enhance the stratum corneum's permeability is to use cocktails of different MPE™s, which it terms MMPE™s.

Nuvo's MMPE™ technology uses special combinations of MPE™s to permeabilize the skin for enhanced delivery of a given drug. Throughout 2006 and 2007, the Corporation used its HTE technology to complete hundreds of thousands of measurements on MMPE™ systems applied to skin in an effort to determine which MMPE™s are most effective. Nuvo has filed patent applications claiming certain high potential MMPE™s and uses of these MMPE™s. Nuvo is currently using its database of MMPE™ measurements to develop some of its topical and transdermal drug candidates. (See "— Topical and Transdermal Drug Delivery – Early Stage Drug Development").

#### High Throughput Experimentation ("HTE")

Skin is complex. The nature of the molecules that comprise the skin, and their structure are such that it is usually very difficult to predict whether a given drug will pass through the skin or the degree to which a given MPE™ might affect its permeability. To obtain such data experiments must be conducted. Such experiments are traditionally slow and costly. HTE enables more measurements to be made, in a given time frame, and usually at a reduced per-measurement cost. Nuvo has pioneered HTE approaches to skin property measurement and now operates, in 'production mode', a number of HTE platforms, including INSIGHT™, STORM™ and TEMPEST™.

With INSIGHT™ the Corporation measures how formulations, typically containing MPE™s or MPE™ cocktails, affect the skin barrier. INSIGHT™ increases the rate at which promising MPE™s or MPE™ cocktails can be identified relative to conventional experiments. With INSIGHT™ Nuvo has created an experimental database of measurements for tens of thousands of MPE™ and MPE™ cocktails, an achievement that would have taken many years to complete using traditional screening methods. It is within this database that Nuvo has discovered MMPE™s, those MPE™ combinations that appear to work synergistically to enhance delivery of a particular drug into or through the skin.

With STORM™ the Corporation measures the dynamics of the effect of formulations on the skin barrier, from about a second after the formulation contacts the skin.

With TEMPEST™ the Corporation measures how formulations affect the overall rate at which a given drug contained in a formulation permeates through the skin.

The data generated from each of the INSIGHT™, STORM™ and TEMPEST™ screening platforms has been compared to conventional data, either from scientific literature or as measured internally to validate the utility of the Corporation's HTE screening platforms. The Corporation believes that these HTE screening platforms provide the Corporation's scientists the ability to make many more experiments on skin in a given period of time than other researchers using traditional methods. The Corporation also has an active program of technology development, directed to continued improvement and expansion of its current HTE platforms, as well as to the innovation of new HTE approaches.

### **Formulation Development Process**

The Corporation's drug development process involves applying its topical and transdermal drug delivery technologies, MMPE™ and HTE, with the expertise and experience of its scientists to formulate topical drugs using existing active pharmaceutical ingredients which have proven efficacy and safety. The targeted characteristics for each drug candidate may include improved delivery, reduced dosage or dosing frequency, lower systemic exposure, as well as significant commercial potential. In contrast to the drug development process for new chemical entities ("NCE"), which can take well over 10 years and cost hundreds of millions of dollars, the Corporation believes the development process for its newly formulated topical versions of existing active pharmaceutical ingredients already approved by the FDA for other routes of administration can be significantly shorter and less costly. Prior to conducting the required pre-clinical, pharmacokinetic and clinical work the Corporation's drug development and testing process involves: detailed research on product specifications that need to be achieved to meet clinical and market requirements; extensive laboratory work including the selection of an appropriate MPE™ or MMPE™ for the targeted active pharmaceutical ingredient; defining the parameters of drug release in vitro; and, developing the final formulations to be tested in human clinical trials.

### **Employees**

As at December 31, 2008, the Corporation had 72 full-time employees.

### **Regulatory Environment and Drug Development Process**

The research, development, manufacture and marketing of pharmaceutical products are subject to regulation by the FDA in the U.S., the TPD in Canada, the EMEA in Europe and comparable regulatory authorities in other foreign countries. These agencies and other federal, state, provincial and local entities regulate the testing, manufacture, safety and promotion and sale of the Corporation's products.

For a pharmaceutical company to launch a new prescription or non-prescription drug, whether innovative (original) or a generic version of a known drug, it must demonstrate to the national regulatory authorities in the countries in which it intends to market the new drug that the drug is both effective and safe for its intended use and population. Depending upon the circumstances surrounding the clinical evaluation of a drug candidate, the Corporation may undertake clinical trials, contract clinical trial activities to contract research organizations or rely upon future partners for such development. Approval of a product by one regulatory authority does not necessarily imply that it can or will be approved by a regulatory authority responsible for a different jurisdiction.

Although only the jurisdictions of the United States, Europe and Canada are discussed in this section, the Corporation also intends to seek regulatory approval in other jurisdictions in the future and will initiate clinical studies where appropriate and cost effective.

### **Canada**

In Canada, all drugs are regulated under the Food and Drugs Act and are enforced by the Therapeutic Products Directorate (“TPD”) of the Government of Canada's Department of Health and Welfare. Activities that are regulated include all non-clinical and clinical trials used in support of marketing approval. In addition, the regulations state that good manufacturing practices (“GMP”) must be adhered to during production of all products intended for human use and to some degree during the development process. The regulatory pathway for a potential drug candidate begins by conducting initial proof-of-concept and preliminary safety studies both in the laboratory and in animals (“Pre-clinical Studies”). After the Pre-clinical Studies are completed, applications to conduct human clinical trials with the drug candidate must be submitted to the TPD. This application is referred to as a Clinical Trial Application (“CTA”). The CTA includes information about the methods of manufacture of the drug and controls associated therewith, and Pre-clinical Studies demonstrating safety and potential efficacy of the drug candidate. The TPD has 30 days in which to notify the Corporation if the application is satisfactory by issuance of a No Objection Letter (“NOL”), after which the Corporation may proceed with clinical trials. In addition, before a clinical trial can commence at each participating clinical trial site, the site's institutional review board/research ethics board (“IRB/REB”) must approve the clinical trial protocol and other related documents.

After completing all required pre-clinical and clinical trials, and prior to selling a novel drug in Canada, the Corporation must submit a New Drug Submission (“NDS”) to the TPD and receive a notice of compliance (“NOC”) to sell the drug. The information contained within the NDS describes the new drug, including the drug's generic and proposed names under which it will be sold; a list describing the quantities and qualities of the ingredients; the method of manufacture, processing, and packaging of the drug; controls in place during the manufacturing operations to determine safety, potency, and purity; stability information; results of non-clinical and clinical trials; intended indications for use of the new drug; and the effectiveness of the new drug when used as intended. If, upon review of the NDS by the TPD, the NDS meets the requirements of Canada's Food and Drugs Act and the regulations thereunder, the TPD will issue the NOC. The TPD has the authority to impose certain post-approval requirements, such as post-market surveillance clinical trials. TPD approval can be withdrawn for failure to comply with any post-marketing requirements or for other reasons, such as the discovery of significant adverse effects.

### **United States**

In the United States, all drugs are regulated under the Code of Federal Regulations (“CFR”) which are enforced by the FDA. The regulations are similar to those in Canada and require that non-clinical and clinical studies be conducted to demonstrate the safety and effectiveness of products before marketing and that the manufacturing be conducted according to GMP. Subsequent to the completion of the Pre-clinical Studies the application to conduct human clinical trials with the drug candidate is submitted to the FDA. It is referred to as an Investigational New Drug (“IND”) application. This application contains similar information to the Canadian CTA, and the FDA has 30 days in which to notify the Corporation if the application is unsatisfactory. If the application is deemed satisfactory, then the Corporation may proceed with administering the medication to humans in clinical studies. As in Canada, before any clinical

trial can commence at each participating clinical trial site, the site's IRB/REB must approve the clinical protocol and other related documents.

After completing all required pre-clinical and clinical trials, and prior to selling a drug in the United States, the Corporation must also comply with NDA procedures required by the FDA. The NDA procedure includes the submission of a package containing similar information to that required in the NDS in Canada to indicate safety and efficacy of the drug and describe the manufacturing processes and controls. FDA approval of the submission is required prior to commercial sale or shipment of the product in the United States. Pre- and/or post-approval inspections of manufacturing and testing facilities are necessary. The FDA may also conduct inspections of the clinical trial sites and the pre-clinical laboratories conducting pivotal safety studies to ensure compliance with Good Clinical Practice ("GCP") and Good Laboratory Practice ("GLP") requirements. Similar to the TPD, the FDA has the authority to impose certain post-approval requirements, such as post-market surveillance clinical trials. In addition, FDA approval can be withdrawn for failure to comply with any post-marketing requirements or for other reasons, such as the discovery of significant adverse effects.

### ***Europe***

In Europe, the evaluation of applications for new medicinal products submitted for European approval is coordinated by the European Medicines Agency ("EMA"), a body of the E.U. The regulations are similar to those in Canada and the United States and require that pre-clinical and clinical studies be conducted to demonstrate the safety and effectiveness of products before marketing, and that the manufacturing be conducted according to GMP. Subsequent to the pre-clinical studies and prior to conducting human clinical trials, a CTA must be submitted to the Competent Authority ("CA") in the country where the clinical trial will be conducted. This application contains similar information to the Canadian CTA and U.S. IND. In Europe, the clinical trials are regulated by the European Clinical Trial Directive (2001/20/EC). As in Canada and the U.S., before a clinical trial can commence at each participating clinical trial site, the site's IRB/REB must approve the clinical protocol and other related documents.

A major difference in Europe, when compared to Canada and the United States, is with the approval process. In Europe, there are two different procedures that can be used to gain marketing authorization in the E.U. The first procedure is referred to as the Centralized Procedure and requires that a single application be submitted to the EMA which, if approved, allows marketing in all countries of the E.U. The second procedure has two options: the first is referred to as the Mutual Recognition Procedure and requires that approval is gained from one Member State after which a request is made to the other Member States to mutually recognize the approval; whilst the second is referred to as the Decentralized Procedure which requires a member state to act as the Reference Member State through a simultaneous application made to other member states.

### ***Drug Development Process***

A potential new drug must first be tested in the laboratory and in several animal species (pre-clinical studies) before being evaluated in humans (clinical studies). Pre-clinical studies primarily involve in vitro evaluations of the therapeutic activity of the drug and in vivo evaluations of the pharmacokinetic, metabolic and toxic effects of the drug in selected animal species. Ultimately, based on data generated during pre-clinical studies, extrapolations will be made to evaluate the potential risks versus the potential benefits of use of the drug in humans under specific conditions of use. Upon successful completion of the pre-clinical studies, the drug

typically undergoes a series of evaluations in humans, including healthy volunteers and patients with the targeted disease.

The activities which must typically be completed prior to obtaining approval for marketing a new drug product in Canada, the United States and Europe may be summarized as follows:

- A. Pre-clinical studies: In the pre-clinical stage of drug development, an investigational drug must be tested extensively in the laboratory to ensure it will be safe to administer to humans. Testing at this stage must provide data showing that the drug is reasonably safe for use in initial, small-scale clinical studies. Depending on whether the compound has been studied or marketed previously, the sponsor may have several options for fulfilling this requirement including:
- (a) compiling existing nonclinical data from past *in vitro* laboratory or animal studies on the compound;
  - (b) compiling data from previous clinical testing or marketing of the drug in a country whose population is relevant to the target population; or
  - (c) undertaking new pre-clinical studies designed to provide the evidence necessary to support the safety of administering the compound to humans.

During pre-clinical drug development, a sponsor evaluates the drug's toxic and pharmacologic effects through *in vitro* and *in vivo* laboratory animal testing. Genotoxicity screening is performed, as well as investigations on drug absorption metabolism, the toxicity of the drug's metabolites, and the speed with which the drug and its metabolites are excreted from the body. In North America sponsors are generally asked, at a minimum, to:

- (a) develop a pharmacological profile of the drug;
  - (b) determine the acute toxicity of the drug in at least two species of animals, and
  - (c) conduct short-term toxicity studies ranging from 2 weeks to 3 months, depending on the proposed duration of use of the substance in the proposed clinical studies.
- B. Filing of an IND or CTA: The pre-clinical results are submitted to the FDA, TPD, or other applicable regulatory body, for approval prior to testing in humans.
- C. Clinical Trials: Clinical trials involve the administration of the drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal, state, and local regulations and requirements, under protocols detailing, for example, the objectives of the trial, the parameters to be used in monitoring safety and the efficacy criteria to be evaluated. Clinical trials to support NDAs or NDSs for marketing approval are typically conducted in three sequential phases, but the phases may overlap.

Phase 1 Trials: Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are closely monitored and may be conducted in

patients, but are usually conducted in healthy volunteer subjects. These studies are designed to determine the metabolic and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and, if possible, to gain early evidence on effectiveness. During Phase 1, sufficient information about the drug's pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid, Phase 2 studies. In cases where the Phase 1 studies are conducted on patients and not on healthy volunteers, it is possible that these studies may show evidence of efficacy typically not obtained until Phase 2 studies. These are referred to as Phase 1/2 trials.

Phase 2 Trials: Phase 2 trials are controlled clinical studies conducted to obtain some preliminary data on the effectiveness of the drug for a particular indication or indications in patients with the disease or condition. This phase of testing also helps determine dosage levels, common short-term side effects and risks associated with the drug.

Phase 3 Trials: Phase 3 trials are large controlled and uncontrolled trials. They are performed after preliminary evidence suggesting effectiveness of the drug has been obtained in Phase 2, and are intended to gather additional information about effectiveness and safety that is needed to evaluate the overall risk-benefit relationship of the drug. These studies provide an adequate basis for extrapolating the results to the general population and transmitting that information in the physician labelling. Phase 2/3 trials refer to a combined trial where efficacy and safety are demonstrated.

- D. Filing of an NDA or NDS: An NDA or NDS filing with the relevant regulatory authority in the United States, Canada, Europe or other pertinent jurisdiction documents the safety and efficacy of the investigational new drug and contains all the information collected during the drug development process including the Pre-clinical studies, CMC and the Clinical Trials. At the conclusion of successful pre-clinical, CMC and clinical testing, this series of documents is submitted to the regulatory authority. The application must present substantial evidence that the drug will have the effect it is represented to have when people use it or under the conditions for which it is prescribed, recommended or suggested in the labelling. Obtaining approval to market a new drug frequently takes between six months and two years after submission of an application to the applicable regulatory authority.

Once the data is reviewed and approved by the appropriate regulatory authorities such as TPD, FDA or EMEA, the drug is deemed ready for sale. These authorities and other applicable regulatory bodies will determine whether the drug will be a prescription or non-prescription product based on factors such as the age and history of the drug, the number of patients having reported adverse effects, and how well the drug is documented with respect to safety and efficacy. Given that innovative (original) drugs have no long-term history of public use, it is unlikely that an innovative drug would be approved in the first instance as a non-prescription product.

After marketing approval for a drug has been obtained, further trials may be required by the regulatory authorities (referred to as Phase 4 trials). Post-marketing trials may provide additional data on safety and efficacy necessary to gain approval for the use of the product as a treatment for clinical indications other than that for which the product was initially tested. These trials may also be used for marketing purposes.

## **Litigation, Regulatory Actions, Contingencies and Other Matters**

### ***Leadenhall Bank & Trust Corporation Limited***

The Corporation's former head office property was subject to a \$2.0 million mortgage (the "Mortgage"). As previously disclosed, the Mortgage balance due is in dispute with Leadenhall Bank & Trust Company Limited ("the Mortgagee"). The Mortgage dispute centers on the calculation and amount of interest owing and was the subject of an Ontario court action (the "Ontario Action") commenced by the Mortgagee in April 2005. The Mortgagee's position is that interest should be calculated at a rate of 2% per month calculated monthly; including interest on late payments; and costs. The Corporation's position is that the Mortgage is null and void and should be discharged, or alternatively, that the interest payable is limited to 5% per annum pursuant to the provisions of the Interest Act (Canada). The Ontario Action was subsequently dismissed by the courts for delay. Subsequent to the filing by the Mortgagee of its Statement of Claim and the Corporation of its Statement of Defense and Counterclaim, a liquidator (the "Liquidator") of the Mortgagee was appointed by the courts of the Bahamas, where the Mortgagee is situated.

In November of 2005, the Corporation negotiated a written agreement (the "Settlement Agreement") with the Liquidator to settle all claims pursuant to the Ontario Action for US\$1.1 million (CDN\$1.2 million) (the "Settlement Amount") payable out of closing funds received on the sale of the Corporation's former head office. The Settlement Agreement is subject to the approval of the Bahamian court that appointed the Liquidator. The Liquidator agreed to seek court approval as soon as possible after signing the Settlement Agreement. The Liquidator did not seek court approval prior to the completion of the head office sale, and in order to allow the sale to proceed, the Liquidator and the Corporation entered into an escrow arrangement (the "Escrow Agreement"). Pursuant to the Escrow Agreement, the Liquidator agreed that upon payment of US\$1.4 million (CDN\$1.6 million) to the Liquidator, to be held in escrow pending court approval of the Settlement Agreement, the Liquidator would deliver a discharge of the Mortgage. It was further agreed that upon approval of the Settlement Agreement by the Bahamian Court \$US1.1 million would be released from escrow and paid to the Liquidator and the balance, \$US0.3 million, would be released to the Corporation. In January 2006, the Liquidator discharged the mortgage, the Corporation completed the sale of its head office and it paid \$US1.4 million (CDN\$1.6 million) into escrow with the Liquidator's Bahamian counsel.

The Liquidator has continually delayed seeking court approval of the Settlement Agreement and has not yet presented it to the Bahamian court for approval. Since April 2006, the Liquidator has indicated that while still intending to present the Settlement Agreement to the court for its consideration, it will not recommend that the court approve it. In addition, in its February 2007 Affidavit, the Liquidator indicates that if the Court does not approve the Settlement Agreement, it will request that the Bahamian court order that all escrowed funds, including the US\$0.3 million be released to it and not to the Corporation. The Liquidator further states that the full amount in escrow is insufficient to retire the mortgage principal plus interest at the alleged interest rate of 2% per month and that it may pursue the Corporation for the deficiency. The Corporation has retained legal counsel in the Bahamas to assist it in securing court approval of the Settlement Agreement and to ensure that if the Settlement Agreement is not approved, that the escrow continues in accordance with the terms of the Escrow Agreement.

A hearing in the Bahamian court was held on March 20, 2007. At this hearing, the Liquidator submitted additional arguments to the Bahamian court requesting that all matters, including those that form the basis of the Ontario Action, be decided by the Bahamian court. While this request was not ruled upon, the judge issued an order that the escrow funds continue

to be held in escrow for at least 90 days to provide the Corporation an opportunity to bring an action in the Bahamian courts for the release of the funds based upon the non-ratification of the Settlement Agreement. The judge retired shortly thereafter and to this date no new judge has been assigned to hear the matter.

In June 2007, as the Corporation was not able to bring its action to release the escrow funds to it before the Bahamian courts its Bahamian legal counsel filed a summons in the Leadenhall liquidation proceedings requesting that the Corporation be granted leave to join the liquidation as an interested party. The Summons was served on the Liquidator in June 2007 and requires that the Corporation be notified if the Liquidator intends to make application to have the escrow funds released to it. Since June 2007, the shortage of commercial judges available to hear the case and a lack of co-operation by the Liquidator the Corporation's Bahamian legal counsel has not been able to obtain a date for a hearing at which a judge will consider the Settlement Agreement. Late in 2008, the Corporation's Bahamian legal counsel informed the Corporation that a commercial court judge was assigned to handle all aspects of the Leadenhall liquidation; however, the Corporation still does not have a date for hearing. In January 2009, the Corporation instructed its Bahamian legal counsel to reinitiate dialogue with the Liquidator's counsel for the purpose of attempting to find a mutually agreeable resolution to all outstanding matters between the Corporation and the Liquidator and to jointly approach the courts to seek approval for any potential resolution of matters.

#### ***Ontario Securities Commission ("OSC")***

In October 2004, the Corporation received a letter from the OSC indicating it was reviewing the disclosures and trading activity of the Corporation and requesting that the Corporation provide, among other things, records pertaining to the FDA and the late-stage or Phase 3 testing of Pennsaid®, as well as the Corporation's May 21, 2004 special warrant financing.

During 2006, the Corporation received a series of letters from the OSC requesting additional information and documentation related to the disclosure of the status of the Corporation's original application to the FDA for approval of Pennsaid®. In these letters, the OSC expressed concerns about the accuracy of the disclosure surrounding the status of the Corporation's NDA with respect to Pennsaid® in the U.S. contained in two prospectuses filed by the Corporation prior to the election of the new Board of Directors and appointment of the current management team in late September 2004. On October 6, 2004, the new Board of Directors and management issued a press release which included corrective statements indicating that the Pennsaid® NDA in the U.S. had been effectively placed on hold pending the development of clinical protocols and the completion of the studies contemplated thereby. The Corporation has co-operated with the OSC throughout their investigation which began shortly after the October 6, 2004 press release was issued.

On April 26, 2007, the Corporation reached a settlement with the OSC. The settlement involves a voluntary independent third party review of the Corporation's disclosure and reporting practices and procedures. The Corporation agreed to implement the recommendations made as a result of this third party review. The settlement also required the Corporation to pay \$15,000 towards the cost of the OSC's investigation. The Corporation could still be subject to civil liability in the event of a determination that there was any misrepresentation in its historical disclosures.

During the third quarter of 2007, the independent third-party review of the Corporation's disclosure and reporting practices and procedures was completed. The report noted that the

Corporation had initiated positive steps to create a culture of compliance with respect to corporate governance and disclosure practices and should continue to build upon its practices and procedures to ensure on-going compliance. The report also provided recommendations to further improve specific areas of corporate disclosure, the most significant of which have been implemented.

The OSC is continuing proceedings against the Corporation's former President and CEO, Rebecca Keeler; however, the Staff of the OSC has advised certain former outside directors of the Corporation that it does not intend to commence any proceedings against them at this time. These former directors made aggregate claims of \$71,000 against the Corporation under the indemnity provisions contained in the Corporate By-Laws for reimbursement of legal costs associated with their involvement in the OSC investigation. The Corporation's insurer denied coverage for these costs and, in May 2007, the Corporation paid the claims in full.

### ***Research Capital Corporation ("RCC")***

On June 7, 2006, the Corporation received a letter from counsel to Research Capital Corporation ("RCC") asserting that as a result of the bought deal equity financing completed by the Corporation on June 20, 2006, RCC was entitled to payment of \$1.5 million and such number of Common Shares equal to 8% of the Common Shares issuable pursuant to an engagement letter for an offering that was contemplated but did not proceed in September 2005. RCC was not involved in the financing. The letter further stated that if the demanded cash payment and Common Shares were not received on or before June 12, 2006 then a court action would commence by RCC against the Corporation. On September 15, 2006, RCC commenced legal proceedings against the Corporation by filing a Statement of Claim with the Ontario Superior Court of Justice. The Statement of Claim claims that RCC is entitled to: (i) damages in the amount of \$1.5 million or alternatively damages of \$1.0 million; (ii) 3 million warrants to purchase Common Shares at a price of \$0.50 and an option to purchase \$5 million of Units of the Corporation or alternatively to (i) and (ii), \$350,000, and in each case interest and costs. Management of the Corporation believes that RCC's claim is without merit. The Corporation filed a Statement of Defence and Counterclaim in October 2006 and intends to vigorously defend its position, although there can be no assurance that the Corporation will be successful in its defence. In November 2006, RCC served its reply and defence to the counterclaim. RCC took no further steps to advance the litigation until December 2007 when the Corporation received RCC's unsworn affidavit of documents. The Corporation assembled its affidavit of documents which was served upon RCC and filed with the court. In November 2008, the Corporation and RCC signed a Full and Final Mutual Release and agreed to dismiss the Claim and Counterclaim without costs. Prior to the Minutes of Settlement and the Full and Final Mutual Release being filed by RCC's legal counsel with the Ontario Superior Court issued an order dismissing the Claim due to delays in proceeding with it. Legal Counsel for the Corporation and RCC have agreed that this dismissal should be withdrawn and replaced by the Minutes of Settlement and the Full and Final Mutual Release and are proceeding to effect this.

### ***Squire Tax Reassessment***

On August 16, 2005, the Corporation sold 100% of the common shares of its subsidiary DHCL (renamed Squire) to Paladin. Under the terms of the share purchase agreement ("SPA") with Paladin, the Corporation provided representations and warranties with respect to the status of the Corporation's tax accounts and its tax assets, which consisted of noncapital losses, investment tax credits and undeducted scientific research and experimental development expenditures. If the amounts represented are incorrect then the Corporation is required to indemnify Paladin for a portion of its losses.

In July and August 2008, Squire received notices of reassessment relating to its taxation years ending August 16, 2005 and July 31, 2006 and 2007 (“the Tax Years”) from the Canada Revenue Agency (“CRA”) containing adjustments related to certain transactions occurring in the tax year ended August 16, 2005 that impact all of the Tax Years. Certain provincial tax authorities have also reassessed certain of the Tax Years and other provincial tax authorities may propose similar adjustments as a result of the CRA reassessments. The notices of reassessment, if they stand, could cause the Corporation to breach certain representations and warranties in the SPA.

The Corporation estimates its potential obligation under the indemnification provisions of the SPA as a result of the reassessments is in the range of \$6 million to \$8 million, including interest and penalties. In addition, the Corporation expects the potential obligation under the indemnity to increase as additional interest accrues and penalties are assessed on the reassessed amounts. The SPA also requires the Corporation to indemnify Paladin for out-of-pocket costs (including attorneys’ and experts’ fees) incurred by Paladin that are caused by the Corporation’s breach of its representations and warranties contained in the SPA.

The Corporation disagrees with the position taken by the CRA and believes it is without merit. Squire is contesting the reassessments through the CRA appeals process and has filed a Notice of Objection with the CRA. The Corporation is participating in this process. An unfavorable resolution could have a material adverse impact on the Corporation’s cash flows.

Squire is a “Large Corporation” under subsection 225.1(8) of the Income Tax Act and as a result the CRA took action to collect 50% of the reassessed amount, \$3.7 million, in September 2008. Squire suggested that it may have a claim against the Corporation pursuant to the SPA for a portion of the \$3.7 million. However, on November 17, 2008, the Corporation and Paladin signed an agreement (the “Letter Agreement”), whereby, the Corporation agreed to provide security (the “Indemnity Security”) for potential indemnity obligations that arise from or relates to the CRA Reassessments to Paladin and to pay half of Paladin’s ongoing out-of-pocket costs to contest the CRA Reassessments. The Indemnity Security charges the same assets as the security provided by the Corporation for the Squire 2008 Debenture (See “Description of Capital Structure – Description of the Squire Debentures”). In exchange, Paladin agreed not pursue any claims against the Corporation for reimbursement of any funds that Paladin may have paid or may be required to pay in connection with the CRA Reassessments while their contestation is continuing, except in circumstances where the Corporation has or is to determined to have become insolvent as defined in the Letter Agreement.

### ***Other Matter***

Rebecca Keeler, Nuvo’s former President and CEO, was terminated in September 2004. The Corporation’s position is that the termination was for cause and no cash payment is owing, and it has made no provision for such payment in its financial results. In the event that Mrs. Keeler’s termination is deemed to have been without just cause, she will be entitled to receive a cash payment of two times her former annual salary. In May 2005, the Corporation received correspondence from Mrs. Keeler’s solicitors stating they do not agree with the Corporation’s position that the termination was for just cause and if a settlement cannot be negotiated, they intend to commence legal action. There has been no correspondence with Mrs. Keeler’s solicitors since May 2005.

## **Reorganizations**

On January 1, 2007, the Corporation completed a short-form amalgamation with certain of its subsidiaries. (See “Nuvo Research Inc. Structure – Corporate Structure”).

During the balance of 2007, the Corporation further simplified its structure through the dissolution of two inactive foreign subsidiaries, Dimethaid S.V. Inc. and Dimethaid (Thailand) Limited and the continuance of Dimethaid International Inc. to Canada and subsequent dissolution and conveyance of its assets to Nuvo Research Inc. and assumptions of its liabilities by Nuvo Research Inc. (See “Nuvo Research Inc. Structure – Corporate Structure”).

## **RISK FACTORS**

An investment in the securities of the Corporation is speculative and involves a high degree of risk including, but not limited to, the following risk factors. Before making an investment decision, investors should carefully consider these risk factors. If any of the factors identified as risks actually occur, the Corporation’s business, results of operation and financial condition could be harmed. However, the risks described below are not the only ones the Corporation faces. Additional risks not currently known to the Corporation or those that it currently believes to be immaterial may also harm the Corporation’s business.

### **Need for Additional Financing**

The Corporation has an ongoing need for substantial capital resources to research, develop, commercialize and manufacture its products and technologies. The Corporation will have only limited participation in Pennsaid® sales revenues in those markets where it has currently been approved. Until the Corporation receives FDA approval for the marketing of Pennsaid® in the United States, has a U.S. marketing partner and a successful commercial launch of Pennsaid® in the U.S., Pennsaid® revenues are expected to be insufficient to provide the capital required to be self-sustaining without the need for future financings. There can be no assurance that the Corporation will have sufficient capital to fund its ongoing operations, satisfy the FDA requirements for the approval of Pennsaid®, consummate a licensing agreement for Pennsaid® with a U.S. marketing partner, have a successful commercial launch of Pennsaid® in the U.S., develop or commercialize any further products based on its topical and transdermal drug delivery or immune system regulation platforms without future financings. There can be no assurance, especially considering the current economic environment, that additional financing will be available on acceptable terms, or at all. If adequate funds are not available, the Corporation will have to substantially reduce or eliminate planned expenditures, terminate or delay clinical trials for its product candidates and curtail product development programs designed to expand the product pipeline. If the Corporation is unable to obtain additional financings to address its cash deficiencies, the Corporation may be unable to continue operations.

### **Dependence on the Approval of Pennsaid®’s NDA in the United States**

The Corporation has invested significant financial resources in the development of Pennsaid®, its primary product that is used to treat the symptoms of OA. The ability of the Corporation to generate significant revenues will depend primarily on the approval of Pennsaid® by the FDA for marketing in the United States, and the successful development and commercialization of this product in the United States. Although Nuvo has other products in development, they are at a very early stage in the drug development process.

Pennsaid® has been approved for sale and marketing in a number of countries, including Canada, several Caribbean nations and a number of European countries including Greece, Italy and the United Kingdom. It has not received FDA approval allowing it to be sold and marketed in the United States.

The Corporation's initial submission for FDA approval to market Pennsaid® in the United States was made in 2001. In August 2002, in response to the Corporation's initial NDA application for Pennsaid®, the FDA sent the Corporation a Non-Approvable Letter, detailing a number of deficiencies in the Corporation's application. In consultation with the FDA, the Corporation designed two new Phase 3 clinical trials, a 12-week efficacy trial and a long-term safety trial and conducted a pharmacokinetic study providing more information on DMSO in order to address the deficiencies cited by the FDA in the Non-Approvable Letter. The Corporation successfully completed all required trials and submitted an amended NDA to the FDA in June 2006.

On December 28, 2006, Nuvo received an Approvable Letter from the FDA for Pennsaid®. In its letter, the FDA indicated that Pennsaid® is approvable subject to Nuvo satisfying certain conditions including the provision of additional nonclinical dermal safety and packaging data. None of the conditions in the Approvable Letter related to the clinical efficacy or the clinical safety of Pennsaid®. Furthermore, none of these conditions had been raised by the FDA in the Non-Approvable Letter of August 2002. The FDA has not requested that Nuvo conduct any additional Phase 3 clinical trials as a condition of approval.

During 2007, the Corporation engaged in communications with the FDA in an effort to clarify the Agency's expectations as outlined in the Approvable Letter. Through these communications, the FDA clarified certain of its requirements for additional information relating to Pennsaid®. Based on the contents of the Approvable Letter and these clarifications, the Corporation completed several Short-Term Studies. In addition, the Corporation concluded it must complete three (3) Long-Term Studies to confirm the dermal and systemic safety of Pennsaid®. The three Long-Term Studies are:

- a six (6) month repeat dose dermal toxicity study (the "Six-Month Tox Study");
- a twelve (12) month repeat dose dermal toxicity study (the "Twelve-Month Tox Study"); and,
- a two (2) year dermal carcinogenicity study (the "Carc Study") preceded by a dose finding trial (the "Carc Dosing Trial").

The FDA confirmed in written minutes of a telephone meeting with the Corporation that the Carc Study can be completed post approval, provided no safety concerns are identified in the Six Month Tox Study or the Twelve-Month Tox Study (together the "Tox Studies"). The Corporation has completed the Tox Studies and based upon its interpretation of the data believes there are no safety concerns such that, as per its agreement with the FDA, the Carc Study may be completed post approval. The Corporation completed the Carc Dosing Trial and in subsequent communication with the FDA during 2008 reached a Special Protocol Assessment Agreement on the Carc Study protocol design. This agreement provides the Corporation with the ability commence the Carc Study. On February 4, 2009, the Corporation filed a complete response amendment to address all of the FDA's concerns raised in the Approvable Letter. Upon accepting the resubmission the FDA set August 5, 2009 as the date under the Prescription Drug User Fee Act (the PDUFA date), by which the FDA will advise Nuvo of its decision regarding Pennsaid®'s approvability; however, there is no guarantee that the FDA will complete its review in this timeframe. If approved by the FDA, Pennsaid® will be

permitted to be sold and marketed in the United States. (See “Narrative Description of the Business – Topical and Transdermal Drug Delivery – Pennsaid®”). However, there can be no assurance, if or when, the FDA will approve the sale or marketing of Pennsaid® in the United States.

If the NDA for Pennsaid® is not ultimately approved by the FDA on August 5, 2009, its business could be materially adversely affected. As an example, the FDA could require the Corporation to provide additional data. If Pennsaid® is not approved by the FDA in a timely matter, the Corporation’s business may be materially harmed and it may impede the Corporation’s ability to continue operations.

### **Patents and Proprietary Technology**

There can be no assurance as to the breadth or degree of protection that existing or future patents or patent applications may afford the Corporation, or that any applications will result in issued patents or that the Corporation’s patents or trademarks will be upheld if challenged. Although the Corporation believes that its products do not, and will not, infringe valid patents or trademarks or violate the proprietary rights of others, except as described elsewhere in this AIF, it is possible that the Corporation’s existing patent or trademark rights may be deemed invalid or that its products may infringe on existing or future patents, trademarks or proprietary rights. If the Corporation’s products infringe the patents or proprietary rights of others, the Corporation may be required to modify or rename its products, or obtain licenses to continue using or selling them. There can be no assurance that the Corporation will be able to do so in a timely manner, upon acceptable terms and conditions, or at all. The failure to do any of the foregoing could have a material adverse effect upon the Corporation. In addition, there can be no assurance that the Corporation will have sufficient financial or other resources to enforce or defend a patent infringement or proprietary rights violation action. Moreover, if the Corporation’s products infringe patents, trademarks or proprietary rights of others, the Corporation could, under certain circumstances, become liable for substantial damages, which could also have a material adverse effect.

The Corporation’s key patents for Pennsaid® expired in May 2004 in the United States, in 2005 in Canada and in 2006 in the European Union. The Corporation has filed patent applications for formulations of its follow up product Pennsaid® Plus and other pain formulations; however, there can be no assurance that these patents will be granted or that they will not infringe the patents of others.

Regardless of the validity of the Corporation’s patents, there can be no assurance that others will be unable to obtain patents or develop competitive non-infringing products or processes that permit such parties to compete with the Corporation.

The Corporation may not be able to protect its intellectual property rights throughout the world as filing, prosecuting and defending patents and trademarks on all of the Corporation’s product candidates, products and product names, when and if they exist, in every jurisdiction would be prohibitively expensive. Competitors may use the Corporation’s technologies and its trademarks in jurisdictions where the Corporation or its partners have not obtained patent and trademark protection. These products may compete with the Corporation’s products, when and if it has any, and may not be covered by any of its or its partners’ patent claims or other intellectual property rights.

The laws of some countries do not protect intellectual property rights to the same extent as the laws of Canada and the United States, 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 favor the enforcement of patents, trademarks and other intellectual property protection, particularly those protections relating to biotechnology and pharmaceuticals, which could make it difficult for the Corporation to stop the infringement of its patents. Proceedings to enforce patent rights in foreign jurisdictions could result in substantial cost and divert efforts and attention from other aspects of the business.

### **Inability to Achieve Drug Development Goals within Expected Time Frames**

From time to time, the Corporation sets targets for and makes public statements regarding its expected timing for achieving drug development goals. These include targets for the commencement and completion of pre-clinical and clinical trials, studies and tests and anticipated regulatory filing and approval dates. These targets are set based on a number of assumptions that may not prove to be accurate. The actual timing of these forward-looking events can vary dramatically from the Corporation's estimates, or they might not be achieved at all, due to factors such as delays or failures in clinical trials or pre-clinical work, scheduling changes at Contract Research Organizations ("CROs"), the need to develop additional data required by regulators as a condition of approval, the uncertainties inherent in the regulatory approval process, delays in achieving manufacturing or marketing arrangements necessary to commercialize product candidates and limitations on the funds available to the Corporation. If the Corporation does not meet these targets, including those which are publicly announced, the ultimate commercialization of its products may be delayed and, as a result, its business could be harmed.

### **Uncertainty of Drug Research and Development**

There can be no assurance that any of the Corporation's product candidates will be successfully developed in a timely manner, or that they will prove to be more effective than products based on existing or new technologies, or that a sufficient number of medical professionals will recommend their use. The risk that a product candidate may fail clinical trials, the Corporation's inability to successfully complete development, or a decision for financial or other reasons to halt development of any product candidate, particularly in instances where significant capital expenditures have already been made, could have a material adverse effect on the Corporation.

The return on the Corporation's investment in Dimethaid AG depends on the successful completion of clinical development and subsequent commercialization of WF10. The results from a Phase 3 AIDS study with WF10 in late-stage AIDS patients were disappointing. Clinical trials and development programs with WF10 for other disease indications including the pancreatic cancer clinical development program could yield similarly disappointing results, further diminishing or eliminating the Corporation's ability to recover its investment in Dimethaid AG.

Most of the Corporation's product candidates are at an early stage in the drug development process and have not been subjected to clinical trials. There can be no assurance that pre-clinical or clinical testing of the Corporation's product candidates will yield sufficiently positive results to enable progress toward commercialization and any such trials will take significant time to complete. Unsatisfactory results may prompt the Corporation to reduce or abandon future testing or commercialization of particular product candidates, and this may have a material adverse effect on the Corporation.

## **Regulatory Environment**

The research, testing, manufacturing, packaging, labelling, approval, storage, selling, marketing and distribution of drug products are subject to extensive regulation in the United States by the FDA, in Canada by the TPD and by similar regulatory authorities in the European Union, Japan and elsewhere, and regulations and requirements differ from country to country. The Corporation is not permitted to market its product candidates in the United States until it receives approval of an NDA from the FDA. Despite the time and expense exerted by the Corporation, failure can occur at any stage.

The process of completing a drug development program and obtaining regulatory approval for a drug will, in general, take several years and require substantial resources. Even after initial approval has been obtained, further research, including post marketing studies, may be required to expand indications covered under the product approvals and labelling. Also, regulatory agencies require post marketing surveillance programs to monitor side effects. Results of post marketing programs may limit or expand additional marketing of the drug. Unexpected safety problems could lead to withdrawal of the drug from the market and possible civil action.

In addition to the regulatory product approval framework, pharmaceutical companies are subject to a number of other regulations covering occupational safety, laboratory practices, environmental protection and hazardous substance control. They may also be subject to existing and future local, provincial, state, federal and foreign regulation, including possible future regulation of the overall industry.

### United States Regulation

The FDA has substantial discretion in the drug approval process. The FDA may delay, limit or deny approval of a drug candidate for many reasons including:

- a drug candidate may not be deemed safe or effective;
- the FDA may not find the data from pre-clinical studies, CMC and clinical trials sufficient;
- the FDA may change its approval policies or adopt new regulations; or
- third-party products may enter the market and change approval requirements.

Even once drug candidates are approved these approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. The FDA may require further testing and surveillance programs to monitor the pharmaceutical product that has been commercialized. Non-compliance with applicable requirements can result in fines and other judicially imposed sanctions, including product seizures, injunction actions and criminal prosecutions

### Canada Regulation

The TPD may deny approval of an NDS if applicable regulatory criteria are not satisfied or may require additional testing. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. The TPD may require further testing and surveillance programs to monitor a

pharmaceutical product which has been commercialized. Non-compliance with applicable requirements can result in fines and other judicially imposed sanctions, including product seizures, injunction actions and criminal prosecutions.

### Additional Regulatory Considerations

There is no assurance that problems will not arise which could delay or prevent the commercialization of the Corporation's products currently under development, or that the TPD, FDA, or other foreign regulatory agencies will be satisfied with the information submitted by the Corporation, including results of clinical trials, to approve the marketing of such products. Certain provincial regulatory authorities in Canada have the ability to determine whether the cost of a drug sold within such province will be reimbursed by a provincial government health plan by listing drugs on formularies. These provincial formularies may affect the prices of drugs sold within provinces and the volume of drugs sold within provinces. In addition to the regulatory approval process, pharmaceutical companies are subject to regulations under provincial, state and federal law, including requirements regarding occupational safety, laboratory practices, environmental protection and hazardous substance control, and may be subject to other present and future local, provincial, state, federal and foreign regulations, including possible future regulations of the pharmaceutical industry. The Corporation cannot predict the time required for regulatory approval, or the extent of clinical testing and documentation that is required by regulatory authorities. Any delays in obtaining, or failure to obtain regulatory approvals in Canada, the United States, Europe or other foreign countries would significantly delay the development of the Corporation's markets and the receipt of revenues from the sale of its products.

### **Risk Related to Clinical Trials**

The Corporation must demonstrate through pre-clinical studies and clinical trials that certain of its products being developed are safe and efficacious before the Corporation can obtain regulatory approval for the commercial sale of such products. The results of pre-clinical studies and previous clinical trials are not necessarily predictive of future results, and the Corporation's current product candidates may not have favourable results in later testing or trials. Pre-clinical tests and Phase 1 and Phase 2 clinical trials are primarily designed to test safety, to study pharmacokinetics and pharmacodynamics and to understand the side effects of products at various doses and schedules. Success in pre-clinical or animal studies and early clinical trials does not ensure that later large-scale efficacy trials will be successful and such success is not necessarily predictive of final results. Favourable results in early trials may not be repeated in later trials and positive interim results do not ensure success in final results. Even after the completion of Phase 3 clinical trials, the FDA, TPD, EMEA or other regulatory authorities may disagree with the Corporation's clinical trial design and interpretation of data, and may require additional clinical trials to demonstrate the efficacy of product candidates.

A number of companies in the biotechnology and pharmaceutical industry have suffered significant setbacks in advanced clinical trials, even after achieving promising results in earlier trials and pre-clinical studies. In many cases where clinical results were not favourable, were perceived negatively or otherwise did not meet expectations, the share prices of these companies declined significantly. Failure to complete clinical trials successfully and to obtain successful results on a timely basis could have an adverse effect on the Corporation's future business and its common share price.

### **Patient Enrolment may not be adequate for current trials or future clinical trials**

The Corporation's future prospects could suffer if it fails to develop and maintain sufficient levels of patient enrolment in its current or future clinical trials. Delays in planned patient enrolment may result in increased costs, delays or termination of clinical trials, which could materially harm the Corporation's future prospects.

### **Obtaining Government and Regulatory Approvals**

The Corporation may encounter difficulties or excessive costs in securing necessary approvals or licenses in Canada and the United States, an obstacle that could delay or prevent the Corporation from marketing its products.

The Corporation may not obtain regulatory approvals in countries outside Canada and the United States. It may be required to incur significant costs in obtaining or maintaining foreign regulatory approvals. Failure to obtain necessary regulatory approvals, the restriction, suspension or revocation of existing approvals or any other failure to comply with regulatory requirements, could have a material adverse effect on the Corporation's business, financial condition and operational results.

### **Changes in Government Regulation**

The business of the Corporation may be adversely affected by such factors as changes in the regulatory environment with respect to intellectual property, regulation, export controls or product marketing approvals. Such changes remain beyond the Corporation's control and have an unpredictable impact.

### **Competition**

The pharmaceutical industry is characterized by evolving technology and intense competition. The Corporation is engaged in areas of research where developments are expected to continue at a rapid pace. Many companies, including major pharmaceutical as well as specialized biotechnology companies, are engaged in activities focused on medical conditions that are the same as or similar to those targeted by the Corporation. The Corporation's success depends upon maintaining its competitive position in the research, development and commercialization of topical and transdermally delivered drug products. Competition from pharmaceutical, chemical and biotechnology companies, as well as universities and research institutes, is intense and expected to increase. Many of these organizations have substantially greater research and development capabilities, experience in manufacturing, marketing, financial and managerial resources, and they represent significant competition.

In addition, since the Corporation's drug development strategy involves applying its topical and transdermal drug delivery technologies and development expertise to formulate topical drugs using existing and unprotected active pharmaceutical ingredients, the Corporation may face additional regulatory risks if any of its competitors are developing similar drug candidates. Under the 1984 United States federal law, the Drug Price Competition and Patent Term Restoration Act, informally known as the "Hatch-Waxman Act" (the "Act"), and C.F.R. 314.108(b)(4) a product filed as a 505(b)(2) application and supported by sponsor initiated clinical studies required as a condition of approval is entitled to three years of exclusivity starting from the effective date of approval or longer if granted either orphan drug exclusivity (21 CFR

314.20-316.36) or pediatric exclusivity (section 505A of the Act). If the Corporation's competitors receive the benefit of exclusivity under this Act for a drug product similar to one the Corporation is developing this period of marketing exclusivity could prohibit the approval of the Corporation's drug candidate in the United States for at least three years from the effective date of approval of the competitor's product. Further, approval or filing of any of the Corporation's future 505(b)(2) applications may be delayed because of patent and exclusivity rights that apply to the listed drug (according to 21 CFR 314.50(i), 314.107, and 314.108 and section 505A of the Act).

### **Pennsaid®**

Several major pharmaceutical companies have developed oral COX-2 selective NSAIDs designed to reduce gastrointestinal side effects associated with other types of NSAIDs. Many of these products have been taken off the market or drug development has stopped in response to safety concerns. Those that remain, represent competition for market share. While the Corporation believes that topical administration gives Pennsaid® a better safety profile than oral NSAIDs and Cox-2 selective medications it may be subject to regulations and regulatory decisions of governing bodies, such as the FDA in the United States, including label warnings that apply to NSAIDs generally.

In the U.S., other topical products for the treatment of medical conditions similar to the indication for Pennsaid® have been available over the counter for many years; however, the first topical prescription NSAIDs were only recently approved and launched and will provide competition for market share. If patients and practitioners believe these recently approved and launched products provide pain relief it may be difficult to convince them to use Pennsaid® or conversely, if they do not believe that they provide pain relief they may create a perception that all topically applied products have similar efficacy, making it more difficult to convince physicians and their patients of the value of Pennsaid®.

Pennsaid® will face competition in the U.S. from at least two other topically applied diclofenac drug products that were approved for marketing in 2007 by the FDA. The FLECTOR® Patch has been approved by the FDA for the topical treatment of acute pain due to minor strains, sprains and contusions and was launched by Alpharma Inc. (subsequently acquired by King Pharmaceuticals, Inc.) in January 2008. The FLECTOR® Patch contains the NSAID diclofenac epolamine. The second drug product, Novartis' Voltaren® Gel 1% which contains the NSAID diclofenac sodium, was approved by the FDA for the relief of the pain of OA of joints amenable to topical treatment, such as the knees and those of the hand and was launched by Endo Pharmaceuticals Inc. in the first half of 2008. Both of these topical products are benefitting from being launched in the U.S. market prior to Pennsaid® and they have achieved respectable sales levels in their first year. In 2008, Health Canada approved Novartis' Voltaren Emulgel™ 1.16% and it has been available in Canada without a prescription since October 2008. In Europe and Asia, several major pharmaceutical companies market these and other topical NSAIDs that compete against Pennsaid® in countries where it is marketed.

In addition to the recently approved products, the Corporation is also aware of other companies that are developing topical NSAID products for the U.S., and other markets. Like Pennsaid®, these drugs may reduce the incidence of some of the systemic side effects associated with oral NSAIDs. These products may also reach the U.S. and other markets before Pennsaid® and, in any event, may present additional competition for Pennsaid®.

The Corporation began exploring formulations to improve upon the original Pennsaid® formulation in late 2004. The Corporation has completed preliminary testing of a new, improved

version of Pennsaid®, currently referred to as Pennsaid® Plus. While no clinical trials of this product have taken place to date, in vitro and in vivo tests have indicated that Pennsaid® Plus may increase the transport of diclofenac, the active therapeutic drug in both original Pennsaid® and Pennsaid® Plus, through the skin with less frequent dosing than Pennsaid® providing Pennsaid® Plus with potential advantages over Pennsaid® and with enhanced patent protection. However, there can be no assurance that Pennsaid® Plus will show clinically significant efficacy, receive patent protection or that it will meet all government regulatory testing requirements.

### **WF10**

Several major pharmaceutical companies are at various stages of developing products targeting the immune system. Some of these products have already been approved for marketing and as such, represent competition for market share.

The Corporation's own experience with WF10 is limited. The last Phase 3 HIV/AIDS trial produced disappointing results and the early-stage pancreatic cancer trial at the University of Heidelberg in Germany took much longer than anticipated to recruit subjects. While the interim analysis of the study results was positive, the open-label study design does not allow the Corporation to draw definitive conclusions about the efficacy of WF10 in the treatment of the targeted indication. As a result of the recruiting issues and the determination that completing the study would not provide more conclusive efficacy data the Corporation terminated the trial in December 2008. The Corporation may not recommence a similar trial and, even if it does undertake further WF10 clinical trials, such trials may not be completed successfully. (See "Narrative Description of the Business — Immune System Regulation — WF10").

### **Operating Losses**

The Corporation has incurred net losses each year since inception. To achieve and maintain profitability, Nuvo must successfully commercialize Pennsaid® in jurisdictions where it has obtained marketing approval, and it must obtain marketing approval for Pennsaid® in other jurisdictions, such as the United States, where it intends to develop and commercialize therapeutic products with industry partners.

There can be no assurance that the Corporation will achieve significant revenues from Pennsaid® sales, or that it will achieve or maintain profitability or that it will obtain additional marketing approval for Pennsaid® in other jurisdictions such as the United States. There can be no assurance that the Corporation will successfully develop and obtain regulatory approval for any other therapeutic product or that it will successfully commercialize such product if it is developed and approved.

Through three separate agreements the Corporation licensed the rights to sell Pennsaid® in Canada to Squire. (See "General Development of the Business – Recent Financing and Corporate Transactions – Dispositions"). These transactions provided the Corporation with upfront payments but subsequently reduced Pennsaid® product sales revenue and gross margins that had been earned previously by the Corporation and were available to fund operations and reduce operating losses.

Researching, developing, producing and marketing new products will require considerable technical and financial resources, while revenues from successfully commercialized products may not be realized for a number of years. Other factors that may materially and unpredictably affect operating results include:

- uncertainties and costs associated with the development and eventual commercialization of new products;
- slow or declining sales growth;
- possible claims of patent infringement or proprietary technology by the Corporation's competitors;
- acquisitions or transfers of technology;
- actions by collaborators;
- development of new collaborative arrangements and the timing of associated research and development; and
- timing and costs of obtaining patents and regulatory approvals for products.

The Corporation may never achieve profitability. Even if it achieves profitability, it may not remain profitable. The Corporation's inability to become and remain profitable could depress the market price of its shares and could impair its ability to raise capital, expand its business, expand its product pipeline or continue its operations.

### **Prolonged Development Time**

It takes considerable time to develop new prescription drug products, to obtain the necessary regulatory approvals permitting sales, to establish appropriate distribution channels and market acceptance, and to obtain insurer reimbursement approvals. This time period is generally from three to more than ten years and it exposes the Corporation to significant risks, including the development of competing products, loss of investor interest, shifting consumer preferences, changes in personnel and new regulatory requirements. During this lengthy period, the Corporation often incurs significant development-related costs without obtaining offsetting revenues.

### **Rapid Technological Change could make Products or Drug Delivery Technologies Obsolete**

Pharmaceutical technologies are subject to rapid and significant technological change. The Corporation expects its competitors will develop new technologies and products that may render the Corporation's products and drug delivery technologies uncompetitive or obsolete. The products and drug delivery technologies of its competitors may be more effective than the products and drug delivery technologies developed by the Corporation. As a result, the Corporation's products may become obsolete before it recovers expenses incurred in connection with their development or realize revenues from any commercialized products.

### **Reimbursement and Product Pricing**

There can be no assurance that Pennsaid® will be successfully commercialized in current markets or that the additional regulatory approvals necessary to commercialize Pennsaid® in other markets will be obtained. In Canada, private health coverage insurers have generally approved reimbursement of Pennsaid® costs, but government health authorities have not approved such reimbursement. The Corporation's ability to realize the full commercial potential of Pennsaid® or other therapeutic products may depend on the extent to which patient

costs are reimbursed by government health administration authorities, private health coverage insurers (outside of Canada) and other organizations. Obtaining reimbursement approval for a product from each government or other third-party payor is a time consuming and costly process that could require the Corporation to provide supporting scientific, clinical and cost effectiveness data for the use of its products to each payor. The Corporation may not have or be able to provide data sufficient to gain acceptance with respect to reimbursement. Even when a payor determines that a product is eligible for reimbursement they may impose coverage limitations that preclude payment for some uses that are approved by the FDA or comparable authorities. In addition, there is a risk that full reimbursement may not be available for the Corporation's products.

Furthermore, even after approval for reimbursement for Pennsaid® is obtained from private health coverage insurers or government health authorities, it may be eliminated at any time. Significant uncertainty exists as to the reimbursement status of newly approved healthcare products and there can be no assurance that third party coverage will be sufficient to give the Corporation an appropriate return on its investment in developing existing or new products. Increasingly, government and other third-party payers are attempting to contain expenditures by limiting coverage and reimbursement levels for new therapeutic products. Inadequate coverage or reimbursement could adversely affect market acceptance of the Corporation's products. Third-party payers increasingly challenge the pricing of pharmaceutical products. Moreover, the trend toward managed healthcare in the United States, the growth of organizations such as health maintenance organizations, and legislative proposals to reform healthcare and government insurance programs, could significantly influence the purchase of healthcare services and products, resulting in lower prices and reduced demand for the Corporation's products.

In some countries, particularly the countries of the E.U., the pricing of prescription pharmaceuticals is subject to government control. In these countries, pricing negotiations with governmental authorities can take considerable time and delay the introduction of a product to the market. To obtain reimbursement or pricing approval in some countries, the Corporation may be required to conduct a clinical trial that compares the cost effectiveness of its product candidate to other available therapies. If reimbursement of the Corporation's product is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, its business could be adversely affected. In addition, any country could pass legislation or change regulations affecting the pricing of pharmaceuticals in ways adverse to the Corporation before or after a regulatory agency approves any of its product candidates for marketing. While the Corporation cannot predict the likelihood of any legislative or regulatory changes, if any government or regulatory agency adopts new legislation or new regulations, the Corporation's business could be harmed.

### **Dependence on Sales and Marketing Partnerships**

The Corporation has limited sales and marketing experience and lacks the financial or other resources to undertake marketing and advertising activities worldwide. Accordingly, the Corporation intends to rely on marketing arrangements, including possible joint ventures, licensing or other third-party arrangements, to distribute its products in all applicable jurisdictions. The Corporation faces, and will continue to face significant competition in seeking appropriate partners and distributors. Moreover, collaboration and distribution arrangements are complex and time consuming to negotiate, document and implement. Therefore, there can be no assurance that the Corporation will be able to find marketing and distribution partners in applicable jurisdictions or be able to enter into any marketing and distribution arrangements on any terms, acceptable or not. Moreover, there can be no assurance that its partners will

dedicate the resources needed to successfully market and distribute the Corporation's products and maximize sales. In addition, under these arrangements: disputes may arise with respect to payments that the Corporation or its partners believe are due under such distribution or marketing arrangements; a partner or distributor may develop or distribute products that compete with the Corporation's products or they may terminate the relationship.

The Corporation has minimal influence in sales and marketing activities for Pennsaid® in Canada, as such decisions are now made by Squire which sells and markets Pennsaid® in Canada. There is no guarantee that Squire will continue to be successful in selling and marketing Pennsaid® in Canada. If it is not, it could have an adverse effect on the Corporation's Canadian product sales and potential royalty income. (See "General Development of the Business – Products – Pennsaid®").

### **Generic Drug Manufacturers**

Regulatory approval for competing generic drugs can be obtained without investing in the same level of costly and time-consuming clinical trials the Corporation has conducted or might conduct in the future. Because of substantially reduced development costs, generic drug manufacturers are often able to charge much lower prices for their products than the original developer. The Corporation may face competition from manufacturers of generic drugs on some of the products it commercializes, since a number of the Corporation's patents have expired. If the Corporation faces generic competition the prices at which the Corporation's products are sold, the royalty rates the Corporation receives and the overall revenues it receives may be substantially reduced. (See "– Patents and Proprietary Technology").

### **Personnel**

The Corporation depends upon certain key members of its scientific and management teams. The loss of any of these individuals could have a material adverse effect on the Corporation. The Corporation does not maintain key-man insurance on any employee.

The Corporation's success depends, in large part, on its ability to continue to attract and retain qualified scientific and management personnel. The Corporation faces intense competition for such personnel. It may not be able to attract and retain qualified management and scientific personnel in the future. Also, it must provide training for its employee base due to the highly specialized nature of pharmaceutical products.

Further, the Corporation expects that its potential expansion into specific areas and activities requiring new or additional expertise, such as in the areas of research and development, pre-clinical studies, CMC work, clinical trials, regulatory approvals, sales and marketing will place additional requirements on management, operational and financial resources. The Corporation expects these demands will require an increase in the number of management and scientific personnel and development of additional expertise by existing personnel. The failure to attract and retain such personnel, or to develop such expertise, could materially adversely affect prospects for its success. In addition, to attract qualified personnel the Corporation may be required to establish offices in different locations. Failure of personnel in different locations to work effectively together could materially adversely affect the Corporation's success.

Given these potential challenges, current personnel may be unable to adapt or may not have the appropriate skills and the Corporation may fail to assimilate and train new employees. Highly skilled employees with the education and training required, especially employees with

significant experience and expertise in drug delivery systems, are in high demand. Once trained, the Corporation's employees may be hired by its competitors.

### **Reliance on Third Parties to Conduct Clinical and Pre-clinical Studies**

The Corporation relies on third parties such as contract research organizations, medical institutions and clinical investigators to enroll qualified patients, conduct, supervise and monitor its clinical trials, conduct pre-clinical studies and complete CMC work. The Corporation's reliance on these third parties for clinical development activities reduces its control over these activities. The reliance on these third parties, however, does not relieve it of its regulatory responsibilities, including ensuring that its clinical trials are conducted in accordance with GCPs and that its pre-clinical studies are conducted in accordance with GLPs. Furthermore, these third parties may have relationships with other entities, some of which may be competitors. In addition, they may not complete activities on schedule, or may not conduct pre-clinical studies or clinical trials in accordance with regulatory requirements or the Corporation's trial design. If these third parties do not successfully carry out their contractual duties or meet expected deadlines the Corporation's ability to obtain regulatory approvals for product candidates may be delayed or prevented.

### **Potential Product Liability**

The Corporation may be subject to product liability claims associated with the use of its products either after their approval or during clinical trials, and there can be no assurance that liability insurance will be available on commercially reasonable terms or at all. Product liability claims might also exceed the amounts, or fall outside, of such coverage. Product liability claims against the Corporation, regardless of their merit or potential outcome, could be costly and divert the Corporation's management's attention from other business matters, or adversely affect its reputation and the demand for its products.

In addition, certain drug retailers require minimum liability insurance as a condition of purchasing or accepting products for retail distribution. Failure to satisfy such insurance requirements could impede the ability of the Corporation or potential partners to achieve broad retail distribution of its products, resulting in a material adverse effect on the Corporation.

### **Ability to Protect Know How and Trade Secrets**

The ability of the Corporation to maintain the confidentiality of its expertise and trade secrets is essential to success. Disclosure and use of the Corporation's expertise and trade secrets, not otherwise protected by patent, are generally controlled under agreements with the parties involved. There can be no assurance, however, that all confidentiality agreements will be honoured, that others will not independently develop equivalent technology, that disputes will not arise over the ownership of intellectual property, or that disclosure of the Corporation's trade secrets will not occur. To the extent that consultants or other research collaborators use intellectual property owned by others while working with the Corporation, disputes may also arise over the rights to related or resulting expertise or inventions.

### **Manufacturing and Supply Risks**

The Corporation purchases key raw materials necessary for the manufacture of its products from a limited number of suppliers around the world. In the case of dimethyl sulfoxide (one of the key ingredients in Pennsaid®) the Corporation has a supply agreement with a single supplier based in the United States to purchase from that supplier all of the Corporation's

requirements for pharmaceutical grade DMSO until October 31, 2012 using the supplier's patented process. It may be difficult to find another manufacturer if the supplier is unable to supply the Corporation with a sufficient amount of dimethyl sulfoxide or if the Corporation is forced for any other reason to find another supplier. It could take another supplier a significant period of time to develop and certify the necessary processes to manufacture the product on terms acceptable to the Corporation. There may not be suppliers that are able to meet the Corporation's volume or quality requirements at a price that is as favourable as those it currently has. Any operating, production or quality problems experienced by these suppliers that result in a reduction or interruption in supply could significantly delay the manufacture and sale of the Corporation's products.

In addition, the FDA and other regulatory agencies, require that raw material manufacturers comply with all applicable regulations and standards pertaining to the manufacture, control, testing and use of the raw materials as appropriate. For the active pharmaceutical ingredient ("API") or critical raw materials depending on the drug product, this means compliance to current GMPs for APIs and submission of all data related to the manufacture, control and testing of the API for quality, purity, identity and stability as well as a complete description of the process, equipment, controls and standards used for the production of the API. This is usually submitted to the FDA in the form of a Drug Master File ("DMF") by the manufacturer and referenced by the sponsor of the NDA. The DMF information and data is reviewed by the FDA as a critical component of the approvability of the NDA.

As a result, in the case where only one supplier of a particular API or critical raw material meets all of the FDA's (or other regulatory agencies) requirements and has a DMF (or similar filing) on file with the FDA the Corporation is at risk should a supplier violate GMP, fail an FDA inspection, terminate access to its DMF, be unable to manufacture product, choose not to supply the Corporation or decide to increase prices. In the case of dimethyl sulfoxide, the Corporation has only one approved supplier for all jurisdictions in which Pennsaid® has been approved. For its API, diclofenac sodium, the Corporation has two approved suppliers for Canada and Europe but only one approved supplier for the United States. For some of the Corporation's other raw materials required to manufacture Pennsaid®, Oxoferin™ and WF10 the Corporation currently has only one approved supplier.

In addition, the Corporation could be subject to various import duties applicable to both finished products and raw materials, and it may be affected by other import and export restrictions as well as developments with an impact on international trade. Under certain circumstances, these international trade factors could affect manufacturing costs (which will, in turn, affect the Corporation's margins) as well as the wholesale and retail prices of manufactured products.

The Corporation's current manufacturing capabilities are limited to its site in Varennes, Québec, which is the sole manufacturer of Pennsaid® for all markets, and its site in Wanzleben, Germany which produces OXO-K993, the active ingredient in WF10 and Oxoferin™. The Corporation has never achieved capacity in these facilities although it has manufactured Pennsaid® and OXO-K993 for existing markets and produced clinical batches. This exposes the Corporation to the following risks, any of which could delay or prevent the commercialization of its products, result in higher costs, or deprive it of potential product revenues:

- The Corporation may encounter difficulties in achieving volume production, quality control and quality assurance, as well as with shortages of qualified personnel. Accordingly, the Corporation might not be able to manufacture

sufficient quantities to meet its clinical trial needs or to commercialize its products.

- The Corporation's manufacturing facilities are required to undergo a satisfactory current GMP inspection prior to regulatory approval and is obliged to operate in accordance with FDA, European and other nationally mandated GMP, which govern manufacturing processes, stability testing, record keeping and quality standards. A failure to establish and follow GMPs and to document adherence to such practices may lead to significant delays in the availability of material for clinical study and may delay or prevent filing or approval of marketing applications for the Corporation's products.
- Changing manufacturing locations would be difficult and the number of potential manufacturers is limited. Changing manufacturers generally requires re-validation of the manufacturing processes and procedures in accordance with FDA, European and other nationally mandated GMPs. Such re-validation may be costly and would be time-consuming. It would be difficult or impossible to quickly find replacement manufacturers on acceptable terms, if at all.

The Corporation's manufacturing facilities are subject to ongoing periodic unannounced inspection by the FDA, and corresponding state and foreign agencies, including European ones, to ensure strict compliance with GMPs and other government regulations. Failure by the Corporation to comply with applicable regulations could result in sanctions being imposed on it, including fines, injunctions, civil penalties, failure of the government to grant review of submissions or market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of product, operating restrictions, facility closures and criminal prosecutions, any of which could harm the Corporation's business.

### **Hazardous Materials and Environmental**

The Corporation's products involve the use of potentially hazardous materials, and as a result it is exposed to potential liability claims and costs associated with complying with laws regulating hazardous waste. Research and development and manufacturing activities involve the use of hazardous materials, including chemicals, and are subject to federal, provincial and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. However, accidental injury or contamination from these materials may occur. In the event of an accident, the Corporation could be held liable for any damages, which could exceed its available financial resources. In addition, the Corporation may be required to incur significant costs to comply with environmental laws and regulations in the future.

### **Litigation and Regulation**

From time to time, during the ordinary course of business, the Corporation is threatened with, or is named as a defendant in various legal proceedings including lawsuits based upon product liability, patent infringement, personal injury, breach of contract and lost profits or other consequential damage claims.

A significant judgment against the Corporation, or the imposition of a significant fine or penalty, or a finding that the Corporation has failed to comply with laws or regulations, or a failure to settle any dispute on satisfactory terms could have a significant adverse impact on the Corporation's ability to continue operations. Additionally, lawsuits and investigations can be

expensive to defend, whether or not the lawsuit or investigation has merit, and the defence of these actions may divert the attention of the Corporation's management and other resources that would otherwise be engaged in running the Corporation's business.

### **Acquisition and Integration of Complementary Technologies or Businesses**

The Corporation may pursue product or business acquisitions that could complement or expand its business. However, it may not be able to identify appropriate acquisition candidates in the future. If an acquisition candidate is identified, the Corporation may not be able to successfully negotiate the terms of any such acquisition or finance such acquisition. Any such acquisition could result in unanticipated costs or liabilities, diversion of management's attention from the core business, the expenditure of resources and the potential loss of key employees, particularly those of the acquired organizations. In addition, the Corporation may not be able to successfully integrate any businesses, products, technologies or personnel that it might acquire in the future, which may harm its business.

To the extent the Corporation issues Common Shares or other rights to finance any acquisition, existing shareholders may be diluted. They may also result in goodwill and other long-lived assets that are subject to impairment tests, which could result in future impairment charges.

### **Losses due to Foreign Currency Fluctuations**

The Corporation anticipates that the majority of the revenue from commercialization of its product candidates may be in currencies other than Canadian dollars. Fluctuation in the exchange rate of the Canadian dollar relative to these other currencies could result in the Corporation realizing a lower profit margin on sales of its product candidates than anticipated at the time of entering into such commercial agreements. Adverse movements in exchange rates could have a material adverse effect on the Corporation's financial condition and results of operations.

### **International Operations**

The Corporation has operations outside of Canada, primarily in Europe and the United States in order to research, develop, market, distribute and manufacture certain of its products and potential products and may expand such operations further in the future. Participation in international markets requires resources and management attention and subjects the Corporation to business risks, including the following:

- different regulatory requirements for approval of its product candidates;
- dependence on local distributors;
- longer payment cycles and problems in collecting accounts receivable;
- adverse changes in trade and tax regulations;
- absence or substantial lack of legal protection for intellectual property rights;
- difficulty in managing widespread operations;
- political and economic instability;

- increased costs and complexities associated with financial reporting; and,
- currency risks.

The occurrence of any of these or other factors may cause the Corporation's international operations not to be successful, could lower the prices at which it can sell its products, or otherwise have an adverse effect on its operating results.

## **Taxes**

Significant judgment is required in determining the Corporation's provision for income taxes, accrual for capital taxes and claims for investment tax credits ("ITCs") related to qualifying scientific research and experimental development ("SR&ED") expenditures. Various internal and external factors may have favorable or unfavorable effects on future provisions for income taxes and the Corporation's effective income tax rate. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, results of audits by tax authorities, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, future levels of R&D spending and changes in overall levels of income before taxes. Furthermore, new accounting pronouncements or new interpretation of existing accounting pronouncements can have a material impact on the Corporation's effective income tax rate.

On August 16, 2005, the Corporation sold 100% of the common shares of its subsidiary DHCL (renamed Squire) to Paladin. Under the terms of the SPA with Paladin, the Corporation provided representations and warranties with respect to the status of the Corporation's tax accounts and its tax assets, which consisted of noncapital losses, investment tax credits and undeducted scientific research and experimental development expenditures. If the amounts represented are incorrect then the Corporation is required to indemnify Paladin for a portion of its losses.

In July and August 2008, Squire received notices of reassessment relating to its taxation years ending August 16, 2005 and July 31, 2006 and 2007 ("the Tax Years") from the CRA containing adjustments related to certain transactions occurring in the tax year ended August 16, 2005 that impact all of the Tax Years. Certain provincial tax authorities have also reassessed certain of the Tax Years and other provincial tax authorities may propose similar adjustments as a result of the CRA reassessments. The notices of reassessment, if they stand, could cause the Corporation to breach certain representations and warranties in the SPA.

The Corporation estimates its potential obligation under the indemnification provisions of the SPA as a result of the reassessments is in the range of \$6 million to \$8 million, including interest and penalties. In addition, the Corporation expects the potential obligation under the indemnity to increase as additional interest accrues and penalties are assessed on the reassessed amounts. The SPA also requires the Corporation to indemnify Paladin for out-of-pocket costs (including attorneys' and experts' fees) incurred by Paladin that are caused by the Corporation's breach of its representations and warranties contained in the SPA.

The Corporation disagrees with the position taken by the CRA and believes it is without merit. Squire is contesting the reassessments through the CRA appeals process and has filed a Notice of Objection with the CRA. The Corporation is participating in this process. An unfavorable resolution could have a material adverse impact on the Corporation's cash flows.

Squire is a "Large Corporation" under subsection 225.1(8) of the Income Tax Act and as a result the CRA took action to collect 50% of the reassessed amount, \$3.7 million, in

September 2008. Squire suggested that it may have a claim against the Corporation pursuant to the SPA for a portion of the \$3.7 million. However, on November 17, 2008 the Corporation and Paladin signed the Letter Agreement, whereby, the Corporation agreed to provide the Indemnity Security for potential indemnity obligations that arise from or relates to the CRA Reassessments to Paladin and to pay half of Paladin's ongoing out-of-pocket costs to contest the CRA Reassessments. The Indemnity Security charges the same assets as the security provided by the Corporation for the Squire 2008 Debenture (See "Description of Capital Structure – Description of the Squire Debentures"). In exchange, Paladin agreed not pursue any claims against the Corporation for reimbursement of any funds that Paladin may have paid or may be required to pay in connection with the CRA Reassessments while their contestation is continuing, except in circumstances where the Corporation has or is to determined to have become insolvent as defined in the Letter Agreement.

### **Debentures not converted into Equity**

As of December 31, 2008, the Corporation had approximately \$6.0 million of outstanding convertible debentures bearing interest at the rates between five and eight percent per annum and due in 2010. In the event that the holders of the convertible debentures elect to receive repayment of the debentures at maturity instead of converting them into Common Shares, the Corporation could be required to make a substantial outlay of cash. The Corporation may not have the cash resources to make this outlay nor may it have the ability to refinance the debentures. The ability to fund repayment of the debentures will depend on many factors including the Corporation's ability to generate cash in the future which is subject to economic, financial, competitive, legislative, regulatory and other factors many of which are and will remain beyond the Corporation's control. The use of the Corporation's cash resources to repay these debentures would also reduce the availability of cash to fund working capital, capital expenditures, R&D, expansion efforts and other general corporate purposes, and limit its flexibility in planning for, or reacting to, changes in its business and the industry in which it operates.

### **Public Company Requirements may Strain Resources and Distract Management**

As a public company, the Corporation is subject to the reporting requirements of the Securities Act (Ontario), as amended, the regulations and rules thereto, including the national and multilateral instruments adopted as rules, decisions, rulings and orders promulgated under the Act, and the published policy statements issued by the OSC, and the listing requirements of the Toronto Stock Exchange. The ever increasing obligations of being a public company will require significant expenditures and will place additional demands on management as the Corporation complies with the reporting requirements of a public company. The Corporation may need to hire additional accounting, financial and legal staff with appropriate public company experience and technical accounting and regulatory knowledge.

### **Volatility of Share Price**

Market prices for pharmaceutical-related securities, including those of the Corporation, have been historically volatile and subject to substantial fluctuations. Future announcements concerning the Corporation or its competitors—including the results of testing, technological innovations, new commercial products, marketing arrangements, government regulations, developments concerning regulatory actions affecting the Corporation's products and its competitors' products in any jurisdiction, developments concerning proprietary rights, litigation, additions or departures of key personnel, cash flow and public concerns about the safety of the Corporation's products and economic conditions and political factors in the United States,

Europe, Canada or other countries—may have a significant impact on the market price of the Common Shares. In addition, there can be no assurance that the Common Shares will continue to be listed on the TSX.

### **Dilution from Further Equity Financing and Declining Share Price**

If the Corporation raises additional funding or completes an acquisition or merger by issuing additional equity securities, such issuance may substantially dilute the interests of shareholders of the Corporation and reduce the value of their investment. The market price of the Corporation's Common Shares could decline as a result of issuances of new shares or sales by existing shareholders of Common Shares in the market, or the perception that such sales could occur. Sales by shareholders might also make it more difficult for the Corporation itself to sell equity securities at a time and price that it deems appropriate

### **Intangible Assets**

The Corporation is required to review the carrying value of its intangible assets for impairment annually or when events change. The Corporation's intangible assets consist of the net book value of patents and patent applications. Management reviews the carrying value based on projected future results. Any impairment in the carrying value results in a write-down of the intangible asset that is charged to income during the period in which the impairment is determined. The write-down of intangible assets may have a material adverse effect on the results of operations in the period in which the write-down occurs.

### **Issue of Preference Shares**

The Corporation's Board of Directors has the authority to issue undesignated preference shares in one or more series and, before issue, to fix the designation of, and the rights and restrictions attached to, the preference shares of each series, without consent from holders of Common Shares. Preference shares could be issued with voting, dividend, liquidation, dissolution, winding-up and other rights superior to those of the holders of Common Shares.

### **Shareholders' Rights Plan**

The Corporation has adopted a shareholder rights plan ("2009 Rights Plan") which among other things, requires anyone who seeks to acquire 20% or more of the Corporation's outstanding Common Shares to make a bid complying with specific provisions contained in the plan. Failure of the acquirer to comply with the provisions of the 2009 Rights Plan can trigger rights held by existing shareholders that may make the acquisition less attractive to the acquirer. (See "Description of Capital Structure – Description of the Common Shares".) The presence of this plan could prevent or delay a change of control and may deprive or limit strategic opportunities for shareholders to sell their shares.

### **Market for Securities**

There is no public market for the Corporation's debentures or warrants and the Corporation does not intend to apply for a listing of its debentures or warrants on any securities exchange. The debentures or warrants may trade at a discount from their initial offering price, depending on prevailing interest rates, the market for similar securities, general economic conditions and the financial condition of the Corporation, and other factors. There can be no assurance as to the liquidity of the trading market for the Corporation's debentures or warrants or that a trading market for the debentures or warrants will, or will not, develop.

## **Securities Industry Analyst Research Reports**

The trading market for the Corporation's common stock is influenced by the research and reports that industry or securities analysts publish about the Corporation. If one or more of these analysts cease coverage of the Corporation or fail to regularly publish reports on the Corporation, it could lose visibility in the financial markets, which in turn could cause the stock price or trading volume to decline. Moreover, if an analyst who covers the Corporation downgrades its stock or if operating results do not meet analysts' expectations, the stock price could decline. Currently, to the Corporation's knowledge, no analysts publish research reports about the Corporation.

## **Compliance with Laws and Regulations Affecting Public Companies**

Any future changes to the laws and regulations affecting public companies, as well as, the required conversion to International Financial Reporting Standards in 2011 by Canadian publicly accountable entities as mandated by the Canadian Accounting Standards Board, compliance with existing provisions of Multilateral Instrument 52-109 – Certification of Disclosure in Issuer's Annual and Interim Filings of the Canadian Securities Administrators and the other applicable Canadian securities laws and regulation and related rules and policies, may cause the Corporation to incur increased costs as it evaluates the implications of new rules and responds to new requirements. Delays, or a failure to comply with the new laws, rules and regulations could result in enforcement actions, the assessment of other penalties and civil suits.

The new laws and regulations may make it more expensive for the Corporation to provide indemnities to the Corporation's officers and directors and may make it more difficult to obtain certain types of insurance, including liability insurance for directors and officers; as such, the Corporation may be forced to accept reduced policy limits and coverage or incur substantially higher costs to obtain the same or similar coverage. The impact of these events could also make it more difficult for the Corporation to attract and retain qualified persons to serve on its Board of Directors, or as executive officers. The Corporation may be required to hire additional personnel and utilize additional outside legal, accounting and advisory services — all of which could cause general and administrative costs to increase beyond what the Corporation currently has planned. The Corporation is continuously evaluating and monitoring developments with respect to these laws, rules and regulations, and it cannot predict or estimate the amount of the additional costs it may incur or the timing of such costs.

The Corporation is required annually to review and report on the effectiveness of its internal control over financial reporting in accordance with Multilateral Instrument 52-109 – Certification of Disclosure in Issuer's Annual and Interim Filings of the Canadian Securities Administrators. The results of this review are reported in the Corporation's Annual Report and in its Management's Discussion and Analysis of Results of Operations and Financial Condition. The Corporation's CEO and CFO are required to report on the effectiveness of the Corporation's internal control over financial reporting.

Management's review is designed to provide reasonable assurance, not absolute assurance that all material weaknesses existing within the Corporation's internal controls are identified. Material weaknesses represent deficiencies existing in the Corporation's internal controls that may not prevent or detect a misstatement occurring which could have a material adverse affect on the quarterly or annual financial statements of the Corporation. In addition, management cannot provide assurance that the remedial actions being taken by the

Corporation to address any material weaknesses identified will be successful, nor can management provide assurance that no further material weaknesses will be identified within its internal controls over financial reporting in future years.

If the Corporation fails to maintain effective internal controls over its financial reporting, there is the possibility of errors or omissions occurring or misrepresentations in the Corporation's disclosures which could have a material adverse effect on the Corporation's business, its financial statements, and the value of the Corporation's common shares.

### **Risks Relating to the Debentures**

The Debentures issued on November 16, 2004 ("November 2004 Debentures"), are unsecured and effectively rank junior to the Corporation's secured indebtedness.

The debenture indenture, dated November 16, 2004, governing the terms of the November 2004 Debentures (the "Debenture Indenture") does not restrict the Corporation or any of its subsidiaries from incurring additional indebtedness or from mortgaging, pledging or charging its assets to secure any indebtedness. It also does not contain any provisions specifically intended to protect November 2004 Debenture holders in the event of a future leveraged transaction involving the Corporation or its subsidiaries.

At the Corporation's option, the November 2004 Debentures may be redeemed after November 16, 2007 and prior to their maturity date at any time, and from time to time, at the prices provided for in the Debenture Indenture, together with any accrued and unpaid interest. November 2004 Debenture holders should assume that this redemption option will be exercised if the Corporation can refinance at a lower interest rate or if it is otherwise in the Corporation's interest.

### **DIVIDENDS**

Dividends are payable on the Common Shares if and when declared by Nuvo's Board of Directors. The Corporation has never paid dividends on the Common Shares and does not expect to do so in the near future.

### **DESCRIPTION OF CAPITAL STRUCTURE**

The Corporation's authorized share capital consists of an unlimited number of Common Shares and an unlimited number of first and second preferred shares, issuable in series of which 314,420,305 Common Shares and no preferred shares were outstanding as of December 31, 2008.

The following is a description of the material characteristics of the Corporation's Common Shares and Preferred Shares including descriptions of outstanding debentures, warrants and other instruments that are convertible or exercisable into Common Shares.

#### **Common Shares**

##### ***Description of the Common Shares***

The holders of Common Shares are entitled to receive notice of any meeting of the Corporation's shareholders and to attend and vote thereat, excepting those meetings at which only those holding another class of shares or a particular series are entitled to vote. Each

Common Share entitles its holder to one vote. Subject to the rights of those holding preferred shares, the holders of Common Shares are entitled to receive on a pro rata basis such dividends as the Board of Directors of the Corporation may declare out of funds legally available. In the event of the dissolution, liquidation, winding-up or other distribution of the Corporation's assets, such holders are entitled to receive on a pro rata basis all the Corporation's remaining assets after payment of all liabilities, subject to the rights of the holders of the preferred shares. The Common Shares carry no pre-emptive or conversion rights. The preceding was a summary of the principal characteristics of the Common Shares. A full description of the Common Shares can be found in the Corporation's Articles of Amalgamation dated January 1, 2007. The Articles of Amalgamation are available on SEDAR at [www.sedar.com](http://www.sedar.com).

#### ***Description of the Common Share Purchase Warrants Issued May 2008***

On May 29, 2008, the Corporation issued an aggregate of 769,230 Paladin Warrants in connection with the May 2008 Financing. (See "General Development of the Business – Recent Financings and Corporate Transactions"). Each Paladin Warrant entitles Paladin to acquire one Common Share at a price of \$0.169 per Common Share (the "Exercise Price") until May 29, 2010. Any unexercised Paladin Warrants will expire and become null and void at 5:00 p.m. (Toronto time) on May 29, 2010. The Paladin Warrants are non-transferable, contain customary anti-dilution protection and adjustment provisions and are not listed on the TSX or any other exchange.

#### ***Description of the Common Share Purchase Warrants Issued July 2007***

On July 13, 2007, the Corporation issued an aggregate of 50,000,000 July 2007 Warrants in connection with a bought deal equity financing. In connection with the offering, the Corporation also issued 5,000,000 underwriter warrants to the underwriters. An additional 2,500,000 July 2007 Warrants are issuable in connection with the exercise of the underwriter warrants. (See "General Development of the Business – Recent Financings and Corporate Transactions"). Each July 2007 Warrant entitles the holder thereof to acquire one Common Share at a price of \$0.30 per Common Share (the "Exercise Price") until July 13, 2009, subject to certain adjustments described hereafter. Notwithstanding the foregoing, during the period from January 21, 2009 until April 3, 2009, the Exercise Price is reduced to \$0.125 per Common Share under the terms of the 2009 Warrant Incentive Program and as fully described in the First Supplemental Warrant Indenture dated January 6, 2009. If a warrant holder does not exercise his or her July 2007 Warrants on or before April 3, 2009, such warrants will continue to be exercisable for Common Shares on the same terms as previously existed. (See "General Development of the Business — Recent Financings and Corporate Transactions").

Any unexercised July 2007 Warrants will expire and become null and void at 5:00 p.m. (Toronto time) on July 13, 2009. The July 2007 Warrants were issued under a warrant indenture (the "2007 Warrant Indenture") between the Corporation and Computershare Trust Company of Canada ("Computershare"). Computershare's principal transfer office in Toronto is the location at which the July 2007 Warrants may be surrendered for exercise, transfer or exchange.

The July 2007 Warrants are transferable and were issued in registered form. The July 2007 Warrants are not listed on the TSX or any other exchange. Warrant certificates were issued for whole July 2007 Warrants only. Holders of the July 2007 Warrants do not, as such, have any voting right or other right attaching to the Common Shares until the July 2007 Warrants are properly exercised and Common Shares issuable upon the exercise of the July

2007 Warrants are issued. No fractional Common Shares will be issued upon the exercise of July 2007 Warrants and in lieu thereof, if applicable, a cash payment will be made based on the then current market price of the Common Shares. Pursuant to the terms of the July 2007 Warrants, subject to applicable law, the Corporation may purchase, by private contract or otherwise, all of or any of the July 2007 Warrants then outstanding and any July 2007 Warrants so purchased will be cancelled.

The 2007 Warrant Indenture (inclusive of the First Supplemental Indenture) provides for adjustment in the number of Common Shares issuable upon the exercise of the July 2007 Warrants and the exercise price per Common Share upon the occurrence of certain events, including:

- (a) the subdivision or consolidation of the outstanding Common Shares;
- (b) the distribution of Common Shares to all holders of Common Shares by way of dividend or otherwise other than an issue of securities to holders of Common Shares who have elected to receive distributions in securities of the Corporation in lieu of receiving cash dividends;
- (c) the issuance of options, rights or warrants to holders of Common shares entitling them to acquire Common Shares or other securities convertible into Common Shares at less than 95% of the then Current Market Price (as defined in the 2007 Warrant Indenture) of the Common Shares; and
- (d) the distribution to all holders of Common Shares of any securities or assets (other than cash dividends and equivalent dividends).

The 2007 Warrant Indenture (inclusive of the First Supplemental Indenture) also provides for adjustment in the class and/or number of securities issuable upon the exercise of the July 2007 Warrants and exercise price per security in the event of the following additional events:

- (a) reclassifications of the Common Shares;
- (b) consolidations, amalgamations, arrangements or mergers of the Corporation with or into any other company or other entity (other than consolidations, amalgamations, arrangements or mergers which do not result in any reclassification of the outstanding Common Shares or a change of the Common Shares into other shares); or
- (c) the transfer of the undertaking or assets of the Corporation as an entirety or substantially as an entirety to another corporation or other entity.

No adjustment in the exercise price or the number of Common Shares purchasable upon the exercise of the July 2007 Warrants will be required to be made unless the cumulative effect of such adjustment or adjustments would result in a change of at least 1% in the prevailing exercise price or a change in the number of Common Shares purchasable upon exercise by at least one one-hundredth of a Common Share, as the case may be.

From time to time the Corporation, without the consent of the holders of the July 2007 Warrants, may amend or supplement the July 2007 Warrants for certain purposes, including curing defects or inconsistencies or making any change that does not adversely affect the interests of the holders of the July 2007 Warrants. Any amendment or supplement to the July

2007 Warrants that adversely affects the interests of the holders of the July 2007 Warrants may only be made by way of “extraordinary resolution” which is defined as a resolution passed at a meeting of the holders of July 2007 Warrants at which there are holders of July 2007 Warrants present in person or represented by proxy representing at least 25% of the aggregate number of the then outstanding July 2007 Warrants and passed by the affirmative vote of holders of July 2007 Warrants representing not less than 66⅔% of the aggregate number of July 2007 Warrants then outstanding represented at the meeting, or rendered by instruments in writing signed by the holders entitled to purchase not less than 66⅔% of the aggregate number of July 2007 Warrants then outstanding.

The foregoing summary of certain provisions of the 2007 Warrant Indenture (inclusive of the First Supplemental Indenture) does not purport to be complete and is qualified in its entirety by reference to the provisions of the 2007 Warrant Indenture and the First Supplemental Indenture.

As at December 31, 2008, there were 50,000,000 July 2007 Warrants outstanding.

### ***Description of the Common Share Purchase Warrants Issued June 2006***

On June 20, 2006, the Corporation issued an aggregate of 12,499,995 June 2006 Warrants in connection with a bought deal equity financing. (See “General Development of the Business – Recent Financings and Corporate Transactions”). Each June 2006 Warrant entitles the holder thereof to purchase one Common Share at a price of \$0.50 per Common Share (“Exercise Price”) until June 20, 2009, subject to certain adjustments described hereafter. Notwithstanding the foregoing, during the period from January 21, 2009 until April 3, 2009, the Exercise Price is reduced to \$0.125 per Common Share under the terms of the 2009 Warrant Incentive Program and as fully described in the Second Supplemental Warrant Indenture dated January 6, 2009. If a warrant holder does not exercise his or her June 2006 Warrants on or prior to April 3, 2009, they will continue to be exercisable for Common Shares on the same terms as previously existed. (See “Narrative Description of the Business — Recent Financings and Corporate Transactions”).

Any unexercised June 2006 Warrants will expire and become null and void at 5:00 p.m. (Toronto time) on June 20, 2009. The June 2006 Warrants were issued under a warrant indenture (the “2006 Warrant Indenture”) between the Corporation and Computershare. Computershare’s principal transfer office in Toronto is the location at which the June 2006 Warrants may be surrendered for exercise, transfer or exchange.

The June 2006 Warrants are transferable and were issued in registered form. The June 2006 Warrants are not listed on the TSX or any other exchange. Warrant certificates were issued for whole June 2006 Warrants only. Holders of the June 2006 Warrants do not, as such, have any voting right or other right attaching to the Common Shares until the June 2006 Warrants are properly exercised and Common Shares issuable upon the exercise of the June 2006 Warrants are issued. No fractional Common Shares will be issued upon the exercise of June 2006 Warrants and in lieu thereof, if applicable, a cash payment will be made based on the then current market price of the Common Shares.

Pursuant to the terms of the June 2006 Warrants, subject to applicable law, the Corporation may purchase, by private contract or otherwise, all of or any of the June 2006 Warrants then outstanding and any June 2006 Warrants so purchased will be cancelled. The 2006 Warrant Indenture (inclusive of all Supplemental Indentures) provides for adjustment in the

number of Common Shares issuable upon the exercise of the June 2006 Warrants and the exercise price per Common Share upon the occurrence of certain events, including:

- (a) the subdivision or consolidation of the outstanding Common Shares;
- (b) the distribution of Common Shares to all holders of Common Shares by way of dividend or otherwise other than an issue of securities to holders of Common Shares who have elected to receive distributions in securities of the Corporation in lieu of receiving cash dividends;
- (c) the issuance of options, rights or warrants to holders of Common shares entitling them to acquire Common Shares or other securities convertible into Common Shares at less than 95% of the then Current Market Price (as defined in the 2006 Warrant Indenture) of the Common Shares; and
- (d) the distribution to all holders of Common Shares of any securities or assets (other than cash dividends and equivalent dividends).

The 2006 Warrant Indenture (inclusive of the all Supplemental Indentures) also provides for adjustment in the class and/or number of securities issuable upon the exercise of the June 2006 Warrants and exercise price per security in the event of the following additional events:

- (a) reclassifications of the Common Shares;
- (b) consolidations, amalgamations, arrangements or mergers of the Corporation with or into any other company or other entity (other than consolidations, amalgamations, arrangements or mergers which do not result in any reclassification of the outstanding Common Shares or a change of the Common Shares into other shares); or
- (c) the transfer of the undertaking or assets of the Corporation as an entirety or substantially as an entirety to another corporation or other entity.

No adjustment in the exercise price or the number of Common Shares purchasable upon the exercise of the June 2006 Warrants will be required to be made unless the cumulative effect of such adjustment or adjustments would result in a change of at least 1% in the prevailing exercise price or a change in the number of Common Shares purchasable upon exercise by at least one one-hundredth of a Common Share, as the case may be.

The Corporation covenants in the 2006 Warrant Indenture that, during the period in which the June 2006 Warrants are exercisable, it will give notice to warrant holders of certain stated events, including events that would result in an adjustment to the exercise price for the June 2006 Warrants or the number of Common Shares issuable upon exercise of the June 2006 Warrants, at least 10 business days prior to the record date or effective date, as the case may be, of such event. From time to time the Corporation, without the consent of the holders of the June 2006 Warrants, may amend or supplement the June 2006 Warrants for certain purposes, including curing defects or inconsistencies or making any change that does not adversely affect the interests of the holders of the June 2006 Warrants. Any amendment or supplement to the June 2006 Warrants that adversely affects the interests of the holders of the June 2006 Warrants may only be made by way of "extraordinary resolution" which is defined as a resolution passed at a meeting of the holders of June 2006 Warrants at which there are holders of June 2006 Warrants present in person or represented by proxy representing at least 25% of the aggregate number of the then outstanding June 2006 Warrants and passed by the

affirmative vote of holders of June 2006 Warrants representing not less than 66⅔% of the aggregate number of June 2006 Warrants then outstanding represented at the meeting, or rendered by instruments in writing signed by the holders entitled to purchase not less than 66⅔% of the aggregate number of June 2006 Warrants then outstanding.

The foregoing summary of certain provisions of the 2006 Warrant Indenture (inclusive of all Supplemental Indentures) does not purport to be complete and is qualified in its entirety by reference to the provisions of the 2006 Warrant Indenture and all Supplemental Indentures.

On November 20, 2006, the Corporation announced that the TSX had approved the 2006 Warrant Incentive Program designed to encourage the early exercise of the June 2006 Warrants. In order to encourage early exercise, Nuvo amended the terms of the June 2006 Warrants so that upon payment of a reduced exercise price of \$0.40 and surrender of the holder's warrant certificate in accordance with applicable procedures, the holder was entitled to receive one Common Share. The Corporation provided the holders of the June 2006 Warrants an exercise period commencing December 11, 2006 and ending January 31, 2007. During the exercise period, 8,705,909 June 2006 Warrants were exercised resulting in gross proceeds to the Corporation of approximately \$3.5 million.

As at December 31, 2008, there were 3,901,898 June 2006 Warrants outstanding.

#### ***Description of the Common Share Purchase Warrants Issued November 2004***

On November 16, 2004, the Corporation issued an aggregate of 40,729,530 November 2004 Warrants in connection with an equity financing. (See "Description of Capital Structure – Description of Debentures"). Each November 2004 Warrant entitles the holder thereof to purchase one Common Share at a price of \$0.48 per Common Share ("Exercise Price") subject to certain adjustments described hereafter. Notwithstanding the foregoing, during the period from January 21, 2009 until April 3, 2009, the Exercise Price is reduced to \$0.125 per Common Share under the terms of the 2009 Warrant Incentive Program and as fully described in the Third Supplemental Warrant Indenture dated January 6, 2009. If a warrant holder does not exercise his or her November 2004 Warrants on or prior to April 3, 2009, they will continue to be exercisable for Common Shares on the same terms as previously existed. (See "Narrative Description of the Business — Recent Financings and Corporate Transactions").

The November 2004 Warrants expire and become null and void at 5:00 p.m. on November 16, 2009, subject to the right of the Corporation to call all or some of the Warrants for exercise if the Call Trading Condition is satisfied.

The November 2004 Warrants were issued under a warrant indenture (the "November 2004 Warrant Indenture") between the Corporation and Computershare. Computershare's principal transfer office in Toronto is the location at which the November 2004 Warrants may be surrendered for exercise, transfer or exchange.

The November 2004 Warrants are transferable and issued in registered form. The November 2004 Warrants are not listed on the TSX or any other exchange. Warrant certificates will be issued for whole November 2004 Warrants only. Holders of the November 2004 Warrants will not, as such, have any voting right or other right attaching to the Common Shares until the November 2004 Warrants are properly exercised and Common Shares issuable upon the exercise of the November 2004 Warrants are issued.

No fractional Common Shares will be issued upon the exercise of November 2004 Warrants and in lieu thereof, if applicable, a cash payment will be made based on the then current market price of the Common Shares. Pursuant to the terms of the November 2004 Warrants, subject to applicable law, the Corporation may purchase, by private contract or otherwise, all of or any of the November 2004 Warrants then outstanding and any November 2004 Warrants so purchased will be cancelled. The November 2004 Warrant Indenture (inclusive of all Supplemental Indentures) provides for adjustment in the number of Common Shares issuable upon the exercise of the November 2004 Warrants, the exercise price per Common Share and the dollar value prescribed in the Call Trading Condition upon the occurrence of certain events, including:

- (a) the subdivision or consolidation of the outstanding Common Shares;
- (b) the distribution of Common Shares to all holders of Common Shares by way of distribution or otherwise other than an issue of securities to holders of Common Shares who have elected to receive distributions in securities of the Corporation in lieu of receiving cash dividends;
- (c) the issuance of options, rights or warrants to all holders of Common Shares pursuant to a rights offering entitling them to acquire Common Shares or other securities convertible into common shares at less than 95% of the then Current Market Price of the common shares; and
- (d) the distribution to all holders of Common Shares of any securities or assets (other than cash dividends and equivalent dividends).

The November 2004 Warrant Indenture (inclusive of all Supplemental Indentures) also provides for adjustment in the class and/or number of securities issuable upon the exercise of the November 2004 Warrants and exercise price per security in the event of the following additional events:

- (a) reclassifications of the Common Shares;
- (b) consolidations, amalgamations, arrangements or mergers of the Corporation with or into any other company or other entity (other than consolidations, amalgamations, arrangements or mergers which do not result in any reclassification of the outstanding Common Shares or a change of the Common Shares into other shares); or
- (c) the transfer of the undertaking or assets of the Corporation as an entirety or substantially as an entirety to another corporation or other entity.

No adjustment in the exercise price or the number of Common Shares purchasable upon the exercise of the November 2004 Warrants will be required to be made unless the cumulative effect of such adjustment or adjustments would result in a change of at least 1% in the prevailing exercise price or a change in the number of Common Shares purchasable upon exercise by at least one one-hundredth of a Common Share, as the case may be.

The Corporation has covenanted in the November 2004 Warrant Indenture (inclusive of all Supplemental Indentures) that, during the period in which the November 2004 Warrants are exercisable, it will give notice to holders of such warrants of certain stated events, including events that would result in an adjustment to the exercise price for the November 2004 Warrants or the number of Common Shares issuable upon exercise of the November 2004 Warrants, at

least 10 business days prior to the record date or effective date, as the case may be, of such event.

In the event that the Call Trading Condition has been satisfied, the Corporation shall have the right, upon 30 days prior written notice (the "Call Notice") given to all holders of November 2004 Warrants following the satisfaction of the Call Trading Condition (the "Notice Period"), to demand (the "Call Demand") that such holders exercise all or a portion of their rights under the November 2004 Warrants. Upon receipt of the Call Notice, the warrant holders must exercise their November 2004 Warrants prior to the expiry of the Notice Period and if such exercise is not made, or only a partial exercise is made, then any and all rights to further exercise with respect to that portion of their November 2004 Warrants shall cease upon the expiry of the Notice Period. In the event that the Corporation makes demand for the exercise of less than all of the outstanding November 2004 Warrants, then such demand shall be made on a pro rata basis to each of the warrant holders. In addition, if the Corporation's Call Demand is for less than all of the outstanding November 2004 Warrants as at the time the Call Demand is made, the Corporation shall not be entitled to make a further Call Demand until three months following the expiry of the last Notice Period and further provided that the Call Trading Condition exists as at the time any subsequent Call Demand is made.

From time to time the Corporation, without the consent of the holders of the November 2004 Warrants, may amend or supplement the November 2004 Warrants for certain purposes, including curing defects or inconsistencies or making any change that does not adversely affect the interests of the holders of the November 2004 Warrants. Any amendment or supplement to the November 2004 Warrants that adversely affects the interests of the holders of the November 2004 Warrants may only be made by way of "extraordinary resolution" which is defined as a resolution passed at a meeting of the holders of November 2004 Warrants at which there are holders of November 2004 Warrants present in person or represented by proxy representing at least 25% of the aggregate number of the then outstanding November 2004 Warrants and passed by the affirmative vote of holders of November 2004 Warrants representing not less than 66 $\frac{2}{3}$ % of the aggregate number of November 2004 Warrants then outstanding represented at the meeting, or rendered by instruments in writing signed by the holders entitled to purchase not less than 66 $\frac{2}{3}$ % of the aggregate number of November 2004 Warrants then outstanding.

The foregoing summary of certain provisions of the November 2004 Warrant Indenture (inclusive of all Supplemental Indentures) does not purport to be complete and is qualified in its entirety by reference to the provisions of the November 2004 Warrant Indenture and the Supplemental Indentures.

On November 20, 2006, the Corporation announced that the TSX had approved the 2006 Warrant Incentive Program designed to encourage the early exercise of the November 2004 Warrants. In order to encourage the early exercise of the warrants, Nuvo amended the November 2004 Warrants so that upon payment of a reduced exercise price of \$0.40 and surrender of the holder's warrant in accordance with applicable procedures, the holder was entitled to receive one Common Share. The Corporation provided the holders of the warrants an exercise period commencing December 11, 2006 and ending January 31, 2007. During the exercise period, 10,449,446 November 2004 Warrants were exercised resulting in gross proceeds to the Corporation of approximately \$4.2 million.

As at December 31, 2008, there were 20,012,494 November 2004 Warrants outstanding.

### ***Description of the Squire Debentures***

On December 21, 2006, Squire exercised its option to sell and market Pennsaid® Plus in Canada. As part of that transaction, the Corporation issued to Squire a \$500,000 convertible debenture bearing interest at 8% per annum, calculated and payable semi-annually in arrears and convertible into Common Shares on the basis of \$0.60 per common share. The maturity date was December 22, 2009 provided that if the Corporation had not commenced a pivotal phase 3 clinical trial for Pennsaid® Plus on or prior to May 21, 2008 (the "Milestone"), then, at Squire's option by Notice to the Corporation, the maturity date shall be May 21, 2008. The Corporation did not achieve the Milestone and Squire demanded repayment whereupon the Corporation repaid the debenture. (See "– Products – Pennsaid®").

On July 7, 2008, in connection with the agreement to amend and restate the Pennsaid® and Pennsaid® Plus licensing, supply and other arrangements in Canada, Squire invested \$2.0 million in the Corporation by way of a two-year convertible debenture (the "Squire 2008 Debenture"). This debenture bears interest at 8% per annum, calculated and payable semi-annually in arrears and is convertible into Nuvo Common Shares at a price of \$0.138 per share. The maturity date is July 7, 2010. Prior to conversion, the debenture is collateralized by revenue from Pennsaid® sales in Europe, a mortgage over Nuvo's manufacturing facility in Québec, a charge on manufacturing assets and inventory in Québec and the Corporation's manufacturing intellectual property rights to the extent required to manufacture and market Pennsaid® in Canada.

Unless an event of default has occurred and is continuing, the Corporation may elect, from time to time, subject to applicable regulatory approval, to satisfy the semi-annual interest payments on the Squire 2008 Debenture through the issuance of a sufficient number of Common Shares to Squire in accordance with the terms of the Squire 2008 Debenture.

The Squire 2008 Debenture may be redeemed in whole or in part from time to time at the option of the Corporation with five (5) days' prior notice at a price equal to their principal amount (the "Redemption Price") plus accrued and unpaid interest thereon up to, but excluding the Redemption Date, provided that the volume weighted average closing price of the Common Shares equals or exceeds \$0.276 for five (5) trading days. (See "– Products – Pennsaid®").

### ***Description of the November 2004 Debentures***

On November 16, 2004 the Corporation completed the sale of 12,800 units at a price of \$1,000 per unit for net proceeds of \$11.2 million. As part of the offering, an additional 4,000 units were issued to Dr. Kühne to satisfy obligations arising from the May 2002 purchase of Oxo Chemie. (See "Nuvo Research Inc. Structure – Corporate Structure – Dimethaid AG and Dimethaid GmbH" and "– Acquisitions – Oxo Chemie AG"). Each unit consisted of one 5% convertible, unsecured debenture (collectively, the "November 2004 Debentures") in the principal amount of \$1,000, maturing on November 16, 2009, plus 1,667 common share purchase warrants (each a "November 2004 Warrant"). Prior to the amendment of the November 2004 Debentures as outlined below, at any time prior to maturity, holders other than Nuvo directors or officers could convert the November 2004 Debentures into Common Shares based on a price of \$0.30 per share (the "Conversion Price") (for directors and officers, the conversion price is \$0.39 per share). Each November 2004 Warrant allows holders to acquire one Common Share at an exercise \$0.48 until November 16, 2009. (See "Description of Capital Structure – Description of the Common Share Purchase Warrants Issued November 2004").

On September 18, 2008, the Corporation announced that over two-thirds of the November 2004 Debenture Holders had, pursuant to a written resolution, agreed to amend certain terms of the November 2004 Debentures. The amendments affect all of the outstanding November 2004 Debentures. The terms were amended, as fully described in the Second Supplemental Indenture dated September 17, 2008, to extend the maturity date of the November 2004 Debentures by one year from November 16, 2009 to November 16, 2010 and to adjust the Conversion Price of all November 2004 Debentures (including those held by directors and officers) to \$0.138.

The following is a summary of the material attributes and characteristics of the November 2004 Debentures as amended. This summary does not purport to be complete and is subject to, and qualified in its entirety by, reference to the terms of the Debenture Indenture and the Supplemental Indentures dated January 1, 2007 and September 17, 2008 (all together the "November 2004 Debenture Indenture").

#### General

The November 2004 Debentures were issued pursuant to the Debenture Indenture dated November 16, 2004 between the Corporation and the Computershare Trust Company of Canada. The Debenture Indenture has subsequently been supplemented by two supplemental indentures dated January 1, 2007 and September 17, 2008 (all together the "November 2004 Debenture Indenture").

The aggregate principal amount of November 2004 Debentures authorized for issue under the November 2004 Debenture Indenture is unlimited. As at December 31, 2008, there was \$4.0 million aggregate principal amount of November 2004 Debentures outstanding. The November 2004 Debentures are issuable only in denominations of \$1,000 and integral multiples thereof. The November 2004 Debentures are due on November 16, 2010. The November 2004 Debentures are not listed on the TSX or on any other exchange.

The November 2004 Debentures bear interest from and including the date of issue at 5.0% per annum, calculated and payable semi-annually in arrears on May 16 and November 16 of each year (each, an "Interest Payment Date"). Interest payments are payable by cash or, at the option of the Corporation, by the issuance and delivery of Common Shares to Computershare Trust Company of Canada (the "Debenture Trustee") for sale on the open market and delivery of a cash amount equal to the amount payable to holders of November 2004 Debentures. (See "– Interest Payment Election").

If the Corporation exercises the Common Share Interest Payment Election (as defined below in "– Interest Payment Election"), the Common Shares issuable will be valued at the closing price of the Common Shares on the TSX on the last Trading Day immediately preceding the applicable Interest Payment Date. Any payment of interest required to be paid on a day that is not a business day will be paid on the next succeeding business day. Interest is computed on a 365-day year (366-day year in the case of leap years).

The November 2004 Debentures are direct obligations of the Corporation and are not secured by any mortgage, pledge, hypothec or other charge. The November 2004 Debenture Indenture does not restrict the Corporation from incurring additional indebtedness for borrowed money or from mortgaging, pledging or charging its properties to secure any indebtedness.

## Conversion Privilege

The November 2004 Debentures are convertible at the holder's option into fully paid and non-assessable Common Shares at any time before the close of business on the earlier of November 16, 2010 (the "Maturity Date") and the business day immediately preceding the date fixed for redemption at the Conversion Price, which, subject to adjustment as summarized below, is a ratio of approximately 7,246 Common Shares per \$1,000 principal amount of November 2004 Debentures (approximately 3,333 Common Shares per \$1,000 principal amount prior to September 17, 2008). Holders converting their November 2004 Debentures will receive accrued and unpaid interest thereon up to, but excluding, the date of conversion. Notwithstanding the foregoing, no November 2004 Debentures may be converted during the five business days preceding and including May 16 and November 16 each year, as the registers of the Debenture Trustee will be closed during such periods.

Subject to the provisions thereof, the November 2004 Debenture Indenture will provide for the adjustment of the Conversion Price in certain events including:

- (a) the subdivision or consolidation of the outstanding Common Shares;
- (b) the distribution of Common Shares to all holders of Common Shares by way of distribution or otherwise other than an issue of securities to holders of Common Shares who have elected to receive distributions in securities of the Corporation in lieu of receiving cash dividends;
- (c) the issuance of options, rights or warrants to holders of Common Shares entitling them to acquire Common Shares or other securities convertible into Common Shares at less than 95% of the then current market price of the Common Shares; and
- (d) the distribution to all holders of common shares of any securities or assets (other than cash dividends and equivalent distributions in securities paid in lieu of cash dividends).

There will be no adjustment of the Conversion Price in respect of any event described in (b), (c) or (d) above if the holders of the November 2004 Debentures are allowed to participate as though they had converted their November 2004 Debentures prior to the applicable record date or effective date. The Corporation will not be required to make adjustments in the Conversion Price unless the cumulative effect of such adjustments would change the Conversion Price by at least 1%.

In the case of a reclassification or a capital reorganization (other than a change resulting from consolidation or subdivision) of the Common Shares or in the case of any consolidation, amalgamation or merger of the Corporation with or into any other entity, or in the case of a sale or conveyance of the properties and assets of the Corporation as, or substantially as, an entirety to any other entity, or a liquidation, dissolution, winding-up of the Corporation or other similar transaction, the terms of the conversion privilege shall be adjusted so that each holder of a November 2004 Debenture shall, after such reclassification, capital reorganization, consolidation, amalgamation, merger, sale, conveyance, liquidation, dissolution, winding up or other similar transaction, be entitled to receive the number of Common Shares, shares of stock, securities or assets as such holder would be entitled to receive if on the effective date thereof, it had been the holder of the number of Common Shares into which the November 2004 Debenture was convertible immediately prior to the effective date of such reclassification, capital reorganization, consolidation, amalgamation, merger, sale, conveyance, liquidation, dissolution, winding up or other similar transaction. No consent of the holders of the November 2004

Debentures will be required in connection with any of the events described in this paragraph and the holders of the November 2004 Debentures will have no voting or other approval rights with respect to any such event.

No fractional Common Shares will be issued on any conversion, but in lieu thereof the Corporation shall satisfy fractional interests by a cash payment equal to the current market price of any fractional interest.

#### Redemption and Purchase

The November 2004 Debentures were not redeemable prior to November 16, 2007. On or after November 16, 2007, and prior to the Maturity Date, the November 2004 Debentures may be redeemed in whole or in part from time to time at the option of the Corporation not more than 60 days' and not less than 30 days' prior notice at a price equal to 102% of their principal amount (the "Redemption Price"), plus accrued and unpaid interest thereon up to, but excluding the Redemption Date, provided that the market price of the Common Shares equals or exceeds 125% of the Conversion Price on the day notice of the proposed redemption is first given to the Debenture Trustee ( the "Redemption Trading Condition").

In the case of redemption of less than all of the November 2004 Debentures, the November 2004 Debentures to be redeemed will be selected by the Debenture Trustee on a pro rata basis or in such other manner as the Debenture Trustee deems equitable.

The Corporation will have the right to purchase November 2004 Debentures in the market, by tender, or by private contract at any price.

#### Payment upon Redemption or Maturity

On redemption or at maturity, the Corporation has the obligation to repay the indebtedness represented by the November 2004 Debentures by paying to the Debenture Trustee in lawful money of Canada an amount equal to the aggregate Redemption Price of the outstanding November 2004 Debentures which are to be redeemed or the principal amount of the outstanding November 2004 Debentures which have matured or have otherwise become due, together with accrued and unpaid interest thereon up to but excluding the redemption date, the Maturity Date or such earlier date as such principal amount becomes due.

#### Interest Payment Election

Unless an Event of Default (as defined below) has occurred and is continuing, the Corporation may elect, from time to time, subject to applicable regulatory approval, to satisfy the Interest Obligation, on any Interest Payment Date by delivering sufficient Common Shares to the Debenture Trustee to satisfy all or any portion of the Interest Obligation in accordance with the November 2004 Debenture Indenture (the "Common Share Interest Payment Election").

The November 2004 Debenture Indenture provides that, upon such election, the Debenture Trustee shall, subject to applicable securities laws (a) accept delivery from the Corporation of Common Shares, (b) accept bids with respect to, and consummate sales of such Common Shares as the Corporation's nominee as the Corporation shall direct in its absolute discretion, (c) invest the proceeds of such sales as the November 2004 Debenture holder's nominee in short-term permitted government securities (as defined in the November 2004 Debenture Indenture) that mature prior to the applicable Interest Payment Date, and use the proceeds received from such permitted government securities, together with any proceeds from

the sale of Common Shares not invested as aforesaid, to satisfy the Interest Obligation, and (d) perform any other action necessary or incidental thereto. The November 2004 Debenture Indenture also provides that the Corporation will issue a press release announcing that it is electing to exercise the Common Share Interest Payment Election concurrently with delivery of notice thereof to the Debenture Trustee.

The November 2004 Debenture Indenture sets forth the procedures to be followed by the Corporation and the Debenture Trustee in order to affect the Common Share Interest Payment Election. If a Common Share Interest Payment Election is made, the sole right of a November 2004 Debenture holder in respect of interest will be to receive cash from the Debenture Trustee out of the proceeds of the sale of Common Shares delivered to the Debenture Trustee pursuant to the Common Share Interest Payment Election (plus any amount received by the Debenture Trustee from the Corporation attributable to fractional Common Shares) in full satisfaction of the Interest Obligation, and the holder of such November 2004 Debentures will have no further recourse to the Corporation in respect of the Interest Obligation. The Common Share Interest Payment Election will not be available for interest payable on the Maturity Date.

Neither the Corporation's making of the Common Share Interest Payment Election nor the consummation of sales of Common Shares will (a) result in the holders of November 2004 Debentures not being entitled to receive on the applicable Interest Payment Date cash in an aggregate amount equal to the interest payable on such Interest Payment Date as determined pursuant to the Common Share Interest Payment Election, or (b) entitle such holders to receive any Common Shares in satisfaction of the Interest Obligation.

The Corporation has undertaken to the OSC that it will not, without the prior consent of the OSC, issue Common Shares pursuant to a Common Share Interest Payment Election. Consequently, the ability of the Corporation to avail itself of the Common Share Interest Payment Election is subject to the prior consent of the OSC.

#### Change of Control of the Corporation

Within 30 days following the occurrence of a Change of Control, the Corporation is required to make an offer in writing to purchase all of the November 2004 Debentures then outstanding (the "Offer"), at the Offer Price.

The November 2004 Debenture Indenture contains notification and repurchase provisions requiring the Corporation to give written notice to the Debenture Trustee of the occurrence of a Change of Control within 30 days of such event together with the Offer. The Debenture Trustee will thereafter mail to each holder of November 2004 Debentures a notice of the Change of Control together with a copy of the Offer to repurchase all of the outstanding November 2004 Debentures.

If 90% or more in aggregate principal amount of the November 2004 Debentures outstanding on the date of the giving of a notice of a Change of Control have been tendered to the Corporation pursuant to the Offer, the Corporation will have the right and obligation to redeem all the remaining November 2004 Debentures at the Offer Price. Notice of such redemption must be given by the Corporation to the Debenture Trustee within 10 days following the expiry of the Offer, and as soon as possible thereafter, by the Debenture Trustee to the holders of the November 2004 Debentures not tendered pursuant to the Offer. Payment of the Offer Price may be limited by the Corporation's current or future debt agreements.

## Events of Default

The November 2004 Debenture Indenture provides that an event of default (“Event of Default”) in respect of the November 2004 Debentures will occur if any one or more of certain prescribed events has occurred and is continuing with respect of the November 2004 Debentures, including, among other things: (i) failure for 10 days to pay interest on the November 2004 Debentures when due; (ii) failure to pay principal or premium, if any, when due on the November 2004 Debentures, whether at maturity, upon redemption, by declaration or otherwise; (iii) certain events of bankruptcy, insolvency or reorganization of the Corporation under bankruptcy or insolvency laws; (iv) an encumbrancer having taken possession of or appointing a receiver for all or substantially all of the property of the Corporation; or (v) default in the observance or performance of any material covenant or condition of the November 2004 Debenture Indenture (including covenants respecting the Corporation’s obligation to comply with the terms of the November 2004 Warrant Indenture and maintain listing of its Common Shares on the TSX) and continuance of such default for a period of 30 days after notice in writing has been given by the Debenture Trustee or by holders of not less than 25% of the outstanding principal amount of November 2004 Debentures to the Corporation specifying such default and requiring the Corporation to rectify the same. If an Event of Default has occurred and is continuing, the Debenture Trustee may, in its discretion, and shall, upon request of holders of not less than 25% in principal amount of the principal amount of outstanding November 2004 Debentures, declare the principal of, premium, if any, and interest on all outstanding November 2004 Debentures to be immediately due and payable. In certain cases, the holders of a majority of the principal amount of the November 2004 Debentures then outstanding may, on behalf of the holders of all November 2004 Debentures, waive any Event of Default and/or cancel any such declaration upon such terms and conditions as such holders shall prescribe.

## Offers for November 2004 Debentures

The November 2004 Debenture Indenture contains provisions to the effect that if an offer is made for the November 2004 Debentures which is a take-over bid for November 2004 Debentures within the meaning of the Securities Act (Ontario) and not less than 90% of the November 2004 Debentures (other than November 2004 Debentures held at the date of the take-over bid by or on behalf of the offeror or associates or affiliates of the offeror) are taken up and paid for by the offeror, the offeror will be entitled to acquire the November 2004 Debentures held by the holders of November 2004 Debentures who did not accept the offer on the terms offered by the offeror.

## Modification

The rights of the holders of the November 2004 Debentures as well as holders of any other series of debentures (collectively, the “holders of debentures”) that may be issued under the November 2004 Debenture Indenture may be modified in accordance with the terms of the November 2004 Debenture Indenture. For that purpose, among others, the November 2004 Debenture Indenture contains certain provisions which (subject to certain exceptions) make it binding on all holders of debentures resolutions passed at meetings of the holders of debentures by votes cast thereat by holders of not less than 66⅔% of the principal amount of the debentures present at the meeting or represented by proxy, or rendered by instruments in writing signed by the holders of not less than 66⅔% of the principal amount of the debentures. In certain cases, the modification will, instead or in addition, require assent by the holders of the required percentage of debentures of each particularly affected series.

In certain circumstances, the Corporation and the Debenture Trustee may amend the November 2004 Debenture Indenture or the November 2004 Debentures for certain purposes, including to (i) cure any ambiguity, defect or inconsistency, provided, however, that the amendment to cure any such ambiguity, defect or inconsistency does not materially adversely affect the rights of holders of November 2004 Debentures; (ii) provide for the assumption by a successor of the Corporation's or the Debenture Trustee's obligations under the November 2004 Debenture Indenture; (iii) make any change to comply with any applicable laws or requirements of any governmental authority relating to trust indentures; (iv) add to the Corporation's covenants or the Corporation's obligations under the November 2004 Debenture Indenture for the protection of holders of November 2004 Debentures; or (v) make any other change that does not adversely affect the rights of holders of November 2004 Debentures.

### ***Shareholder Rights Plan***

The Corporation instituted a shareholder rights plan (the "Rights Plan") in 1992 to provide the Board of Directors with sufficient time to consider and, if appropriate, to explore and develop alternatives for maximizing shareholder value if a takeover bid is made for the Corporation, and to provide every shareholder with an equal opportunity to participate in such a bid. On October 21, 2003, shareholders approved various amendments and a restatement of the Rights Plan and the continuation of the existing Rights Plan (the "2003 Plan") for another five years. The terms of the 2003 Plan are set out in the shareholder rights plan agreement (the "2003 Rights Agreement") dated as of December 16, 1992 (amended and restated on October 21, 2003, previously amended and restated on September 28, 1998), between the Corporation and CIBC Mellon Trust Company of Canada as rights agent (the "Rights Agent"). The Board of Directors determined it appropriate and in the best interests of the shareholders that the 2003 Rights Agreement be amended to continue the Corporation's rights plan for another five years. Such continued plan, which was approved by the shareholders of the Corporation at its 2008 Annual General Meeting, is referred to as the "2008 Rights Plan".

The purpose of the 2008 Rights Plan is the same as the 2003 Plan: to provide some protection to shareholders of the Corporation from unfair take-over strategies, including the acquisition of control of the Corporation by a bidder in a transaction or series of transactions, that does not treat all shareholders equally or fairly or afford all shareholders an equal opportunity to share in the premium paid upon an acquisition of control. The 2008 Rights Plan is not intended to prevent all unsolicited take-over bids for the Corporation and will not do so, but rather, is designed to encourage potential bidders to make permitted bids or negotiate take-over proposals with the Board of Directors which they consider are in the best interests of the Corporation and to protect the Corporation's shareholders against being coerced into selling their shares at less than fair value.

Shareholder rights plans continue to be adopted by a large number of publicly held corporations in Canada and the United States. The terms of the 2008 Rights Plan are similar to those recently adopted by other major Canadian companies.

The following is a summary of the principal terms of the 2008 Rights Plan, which is qualified in its entirety by reference to the text of the 2008 Rights Plan. The 2008 Rights Plan is available on SEDAR at [www.sedar.com](http://www.sedar.com).

#### **Rights Prior to Separation Time**

Rights ("Rights") were issued on commencement of the 2003 Plan to all holders of Common Shares of the Corporation. Rights cannot be exercised prior to the Separation Time.

Under the 2008 Rights Plan, the Rights were reconfirmed and the Corporation reconfirmed its authorization to continue the issuance of Rights to all holders of Common Shares of the Corporation. Until the Separation Time, the Rights will be evidenced only by the register maintained by the Rights Agent and will be transferred with and only with the associated Common Shares. Until the Separation Time, or the earlier termination or expiration of the Rights, each new share certificate issued after the record date for the issuance of the Rights, upon transfer of existing Common Shares or the issuance of additional Common Shares, will display a legend incorporating the terms of the 2008 Rights Plan by reference.

#### Separation Time

The Rights will separate and trade apart from the Common Shares after the Separation Time, at which time separate certificates evidencing the Rights will be mailed to the holders or record of common shares. "Separation Time" means the close of business on the tenth business day after the earlier of (i) the first date of a public announcement of facts indicating that a person has become an Acquiring person, (ii) the commencement of, or first public announcement of the intent of any person, other than the Corporation or any corporation controlled by the Corporation, to commence a Take-over Bid or (iii) the date upon which a Permitted Bid ceases to be a Permitted Bid or, in any circumstances, such later date as may be determined by the Board, acting in good faith. After the Separation Time and prior to the occurrence of a Flip-in Event, each Right entitles the holder to acquire one common share upon payment of an Exercise Price of \$50.00.

#### Acquiring Person and Flip-in Event

An "Acquiring Person" is generally, a person who beneficially acquires 20% or more of the outstanding voting shares of the Corporation. The 2008 Rights Plan provides certain exceptions to that rule, including a person who acquires 20% or more of the outstanding Common Shares through a Permitted Bid, pursuant to certain other exempt acquisitions, or in its capacity as Investment Manager, Trust Corporation, Plan Trustee or Statutory Body, provided in these latter instances, that the person is not making or proposing to make a Take-over Bid. The term Acquiring Person does not include the Corporation or any corporation controlled by the Corporation. A "Flip-in Event" occurs when any person becomes an Acquiring Person, at which time each Right will convert into the right to purchase from the Corporation, upon exercise, a number of Common Shares having an aggregate Market Price on the date of the Flip-in Event equal to twice the Exercise Price for an amount in cash equal to the Exercise Price.

#### Permitted Bid

A Flip-in Event does not occur if a take-over bid is a Permitted Bid. A Permitted Bid is a Take-over Bid, made by a means of a Take-over Bid circular, which among other things:

1. is made to all holders of record of Common Shares as registered on the books of the Corporation (other than the Offeror and the Offeror's Affiliates, Associates and persons acting jointly or in concert with any of them);
2. contains, and the take-up and payment for Common Shares tendered or deposited is subject to, an irrevocable and unqualified condition that no Common Shares will be taken up or paid for pursuant to the Take-over Bid prior to the close of business on a date which is not less than 120 days following the date of the Take-over Bid;

3. contains irrevocable and unqualified provisions that all Common Shares may be deposited pursuant to the Take-over Bid at any time prior to the close of business on the date of first take-up or payment for Common Shares under the bid and that all Common Shares deposited pursuant to the Take-over Bid may be withdrawn at any time prior to the close of business on such date;
4. contains an irrevocable and unqualified condition that the number of Common Shares deposited to the Take-over Bid and not withdrawn at the close of business on the date of first take-up or payment for Common Shares under the bid must constitute more than 50% of the then outstanding Common Shares held by shareholders independent of the Offeror; and
5. contains an irrevocable and unqualified provision that, should the condition referred to in clause 4 be met, the Take-over Bid will be extended on the same terms for a period of not less than 10 days from the date of first take-up or payment for Common Shares under the bid.

The 2008 Rights Plan also provides for a "Competing Permitted Bid", which is a Take-over Bid, made during another Permitted Bid, that satisfies all of the requirements of a Permitted Bid other than the requirements of clause 2. The competing Permitted Bid may not expire earlier than the date of the Permitted Bid.

#### Take-over Bid

A Take-over Bid is defined in the 2008 Rights Plan as an offer to acquire Common Shares or securities convertible into Common Shares, where the Common Shares subject to the offer to acquire, together with the Common Shares into which the securities subject to the offer to acquire are convertible, and the Offeror's securities, constitute in the aggregate 20% or more of the outstanding Common Shares at the date of the offer.

#### Redemption and Waiver

At any time prior to the occurrence of a Flip-in Event, the Board may, at its option, redeem all, but not part, of the outstanding Rights at a redemption price of \$0.00001 per Right, subject to appropriate adjustment in certain events. The Board may, at its option, after the occurrence of a Flip-in Event, waive the application of the Flip-in Event provisions to a transaction that would otherwise be subject to those provisions.

#### Amendments

The Corporation may, from time to time, supplement or amend the 2008 Rights Plan in order to cure any ambiguity or to correct or supplement any provisions contained in the agreement which may be inconsistent with any other provision thereof or otherwise defective. The Corporation may also amend the agreement without the approval of any holders of Rights or Common Shares to make any changes which the Board may deem necessary or desirable and as shall not materially adversely affect the interests of the holders of Rights generally, provided that no such supplement or amendment shall be made to the provisions relating to the Rights Agent except with the concurrence of the Rights Agent.

## Expiry of Rights

All rights will expire unless continuance of the 2008 Rights Plan is approved by a majority vote of Independent Shareholders at the annual meeting of the shareholders of the Corporation to be held in 2013.

## **Share Incentive Plan**

Under the Corporation's Second Amended and Restated Share Incentive Plan (the "Share Incentive Plan") there are three sub plans: the Share Purchase Plan, the Share Option Plan, and the Share Bonus Plan. The original plan was amended and restated effective September 21, 2005 when shareholders of the Corporation approved an amendment changing the maximum number of Common Shares that may be issued under the plan from a fixed maximum number to a fixed maximum percentage. The amendment changes the maximum number of Common Shares that may be issued under the Share Incentive Plan to a fixed maximum percentage of 15% of the Corporation's outstanding Common Shares (on a fully-diluted basis other than stock options) from time to time. The Common Shares that may be issued under the plan are allocated to the three sub-plans as follows: Share Option Plan 10%, Share Purchase Plan 3%, and Share Bonus Plan 2%. As the Share Incentive Plan is a "rolling plan", the TSX requires that it, along with any unallocated options, rights or other entitlements receive shareholder approval at the Corporation's annual meeting every three years. At the Annual and Special Meeting of Common Shareholders of the Corporation held on May 1, 2008 the Common Shareholders approved an ordinary resolution affirming, ratifying and approving the Share Incentive Plan and approving all of the unallocated Common Shares issuable pursuant to the Share Incentive Plan.

### Share Purchase Plan

Under the Share Purchase Plan eligible officers, employees or consultants of the Corporation or its affiliates may contribute up to 10% of their annual base salary to the plan to purchase Common Shares. The Corporation matches each participant's contribution by issuing Common Shares having a value equal to the aggregate amount contributed by each participating employee. As at December 31, 2008 the number of Common Shares available for issuance under the Share Purchase Plan was 5,702,003.

### Share Option Plan

Under the Share Option Plan the Corporation may grant options to purchase common shares to officers, directors, employees or consultants of the Corporation or its affiliates. Options issued under the Share Option Plan are granted for a term not exceeding ten years from the date of grant. Under the provisions of the Share Incentive Plan, the exercise price of all Common Share options shall not be less than the closing price of the Common Shares on the last trading date immediately preceding the grant date of the option. As at December 31, 2008 30,879,394 Common Share options were issued and outstanding and the number of unoptioned Common Shares available to be reserved was 8,905,113. Any unexercised Common Share options that are surrendered, terminate or expire without being exercised become unoptioned and are available for reissuance under the Share Option Plan.

### Share Bonus Plan

Under the Share Bonus Plan, the Corporation can issue Common Shares to eligible directors, officers or employees of the Corporation or its affiliates as a discretionary bonus. In

addition, consultants are also eligible to receive Common Shares in lieu of cash compensation. As at December 31, 2008 the number of Common Shares available for issuance under the Share Bonus Plan was 6,337,739.

## Preferred Shares

### *Description of the Preferred Shares*

Preferred shares may be issued from time to time in one or more series, the number, designation, rights, privileges, restrictions and conditions of which are to be determined by the Board of Directors. The Preferred Shares are entitled to priority over the Common Shares with respect to the payment of dividends and distributions in the event of the dissolution, liquidation or winding-up of the Corporation. Except as required by law, the holders of first preferred shares as a class, and holders of second preferred shares as a class are not entitled to receive notice of, attend or vote at any meeting of the Corporation's shareholders. The preceding was a summary of the principal characteristics of the Preferred Shares. A full description of the Preferred Shares can be found in the Corporation's Articles of Amalgamation dated January 1, 2007. The Articles of Amalgamation are available on SEDAR at [www.sedar.com](http://www.sedar.com).

## MARKET FOR SECURITIES

The Common Shares are listed and posted for trading on TSX under the symbol NRI. The Common Shares are also traded on the Unofficial Regulated Markets of many German stock exchanges including the Berlin, Frankfurt, Munich and Stuttgart Stock Exchanges and the XETRA electronic trading system of the Deutsche Börse.

The following table provides information on the monthly price range and trading volume for the Common Shares on the TSX during the year ended December 31, 2008:

<u>Month</u>	<u>High</u>	<u>Low</u>	<u>Volume (000s)</u>
January 2008	\$0.11	\$0.08	13,491
February 2008	\$0.125	\$0.085	19,600
March 2008	\$0.10	\$0.08	8,205
April 2008	\$0.10	\$0.09	4,670
May 2008	\$0.21	\$0.09	46,411
June 2008	\$0.195	\$0.125	16,319
July 2008	\$0.145	\$0.12	6,153
August 2008	\$0.175	\$0.14	6,634
September 2008	\$0.165	\$0.12	6,886
October 2008	\$0.13	\$0.075	11,296
November 2008	\$0.12	\$0.08	7,398
December 2008	\$0.105	\$0.085	4,761

## DIRECTORS AND OFFICERS

The following table sets forth the name, municipality of residence, position with the Corporation and principal occupation of each director and executive officer of the Corporation. Directors of the Corporation hold office until the next annual shareholders' meeting or until successors are duly elected or appointed.

<b>Name and Residence</b>	<b>Principal Occupation</b>	<b>Director Since</b>	<b>Number of Common Shares Beneficially Owned</b>	<b>Value of November 2004 Convertible Debentures Held (\$)</b>	<b>Number of November 2004 Warrants Held</b>
Daniel H. Chicoine <sup>(7)</sup> Ontario, Canada	Chairman of the Board of the Corporation	September 21, 2004	771,626	300,000 <sup>(5)</sup>	500,100 <sup>(6)</sup>
David A. Copeland <sup>(4)(9)</sup> Ontario, Canada	Private Investor; Member of the Board of directors of various private companies	September 21, 2004	Nil	100,000 <sup>(5)</sup>	166,700 <sup>(6)</sup>
Anthony E. Dobranowski <sup>(1)(3)(8)</sup> Ontario, Canada	Private Business Consultant	September 21, 2004	150,000	Nil	Nil
Dr. Henrich R.K. Guntermann Aachen, Germany	President and Chief Executive Officer of the Corporation	September 21, 2004	Nil	Nil	Nil
Dr. Klaus von Lindeiner <sup>(1,3)</sup> Munich, Germany	Private Business Consultant	September 21, 2004	50,000	Nil	Nil
John C. London Ontario, Canada	Vice Chairman and Secretary of the Corporation	September 21, 2004	404,570	100,000 <sup>(5)</sup>	166,700 <sup>(6)</sup>
Dr. Jacques Messier <sup>(2)</sup> Ontario, Canada	Director of the Veterinary Teaching Hospital, University of Saskatchewan	September 21, 2004	950	Nil	Nil
James Moulds Ontario, Canada	Vice President, Finance and Chief Financial Officer of the Corporation	N/A	1,200,000	Nil	Nil

Notes:

- (1) Member of Compensation and Corporate Governance Committee.
- (2) Chairman of the Compensation and Corporate Governance Committee.
- (3) Member of Audit Committee.
- (4) Chairman of the Audit Committee
- (5) November 2004 Debentures are convertible into Common Shares at a conversion price of \$0.138 per share. Prior to conversion, they bear interest at an annual rate of 5.00%, calculated and payable semi-annually in arrears on May 16 and November 16. The Debentures mature on November 16, 2010. (See "Description of Capital Structure – Description of the November 2004 Debentures").
- (6) Each November 2004 Warrant allows holders to acquire one Common Share at a price of \$0.48 until November 16, 2009. In accordance with the rules of the TSX, insiders are not eligible to participate in the 2009 Warrant Incentive Program. (See ""Description of Capital Structure – Description of the November 2004 Debentures"" and "Description of Capital Structure – Description of the Common Share Purchase Warrants Issued November 2004").
- (7) Dan Chicoine was a director of NRI Industries Inc. ("NRI"), a company primarily involved in the manufacture of rubber and plastic components for automotive and industrial applications, until August 23, 2006, when he resigned. This company filed for protection pursuant to the Companies' Creditors Arrangement Act on September 5, 2006. On April 27, 2007, subsequent to the sale of substantially all of the assets of NRI, the CCAA proceedings were terminated and NRI filed its assignment into bankruptcy and in July 2008 the government cancelled the Corporation for cause.
- (8) Anthony Dobranowski is a trustee of Heating Oil Partners Income Fund. Subsequent to certain of its subsidiaries filing for creditor protection in the U.S. and Canada, the units of the fund were delisted from the Toronto Stock Exchange on November 7, 2005. In March 2006, the OSC issued an issuer cease trade order in respect of the units of the fund and it remains in default with the OSC. The debtors joint plan of reorganization was approved by the U.S. bankruptcy court on June 26, 2006 and Heating Oil Partners Income Fund relinquished all equity interests in the reorganized subsidiaries under the approved plan of reorganization.
- (9) David Copeland was Chairman of the Board of Triton Electronik, a group of Canadian companies primarily involved in electronic contract design and manufacturing service, until January 2009, when he resigned. This group of companies filed for protection pursuant to the Companies' Creditors Arrangement Act on January 28, 2009.

Each of the directors of the Corporation has been engaged for more than five years in his present principal occupation or in other capacities with the corporation or organization (or predecessor thereof) in which he currently holds his or her principal occupation, with the exception of the following: Henrich Guntermann who previous to joining the Corporation held the position of President of BioAlliance AG, a German-based life sciences private equity and consulting firm; Daniel H. Chicoine who prior to joining the Corporation from 2003 to 2004 was Vice-President, Finance and Chief Financial Officer of Cosma International, a division of Magna International Inc. ("Magna"), an international automotive parts manufacturer; John C. London, who previous to joining the Corporation from 2003 to 2004 was President and Chief Executive Officer of PowerCart Systems Inc, a designer and manufacturer of battery equipped workstations for wireless devices; and Dr. Jacques Messier who from 2003 to 2004, was president of the National Income Protection Plan, a start-up company specializing in the management of short-term disability, from 2004 to 2007, was general manager of The Semex Alliance, a developer and marketer of genetic technologies, products and services, and since 2008, is Director of the Veterinary Teaching Hospital at the University of Saskatchewan ; and Anthony E. Dobranowski who from 1995 to 2005 held various positions as Vice Chairman, President, Executive Vice President and Chief Financial Officer of Tesma International Inc., a publicly traded subsidiary of Magna and from 2005 to September 2007 was a Vice President of Magna.

As at December 31, 2008, the directors and executive officers of Nuvo as a group beneficially owned, directly or indirectly, or exercised control or direction of 0.8% of the Corporation's Common Shares. (6.7% assuming all potentially dilutive instruments were exercised or converted).

## **LEGAL PROCEEDINGS AND REGULATORY ACTIONS**

See "Narrative Description of the Business – Litigation, Regulatory Actions, Contingencies and Other Matters".

## **TRANSFER AGENT**

The transfer agent and registrar for the Common Shares is CIBC Mellon Trust Company, P.O. Box 7010, Adelaide Street Postal Station, Toronto, Ontario, Canada M5C 2W9.

The transfer agent for the November 2004 Debentures, the November 2004 Warrants, the June 2006 Warrants and the July 2007 Warrants is Computershare Trust Company of Canada, 100 University Avenue, 8th Floor, North Tower, Toronto, Ontario, M5J 2Y1.

## **AUDIT COMMITTEE**

### **Charter of the Audit Committee**

The Audit Committee of the Corporation's Board of Directors has developed its Charter, the text of which is set forth in Appendix I to this Annual Information Form.

### **Composition of the Audit Committee**

The Audit Committee comprises three members, David A. Copeland, Anthony E. Dobranowski and Dr. Klaus von Lindeiner. Each member is independent and financially literate as defined in Multilateral Instrument 52-110 - Audit Committees.

### **Relevant Education and Experience of Audit Committee Members**

In addition to each member's general business experience, the education and experience relevant to the performance of Audit Committee responsibilities are set forth below.

#### *David A Copeland*

Mr. Copeland is a Chartered Accountant. He holds a Bachelor of Mathematics degree and has been the chief financial officer of a major public Canadian company.

#### *Anthony E. Dobranowski*

Mr. Dobranowski is a Chartered Accountant. He holds a Bachelor of Science Degree, a Masters of Business Administration Degree and has been the chief financial officer and president of a major public Canadian company.

#### *Dr. Klaus von Lindeiner*

Dr. von Lindeiner holds a law degree from the University of Geneva and has been the chief financial officer of two multinational European based corporations.

### **Audit Fees**

BDO Dunwoody LLP was appointed as Auditors of the Corporation by the Audit Committee and the Board of Directors on December 16, 2005 following the resignation of Schwartz Levitsky Feldman LLP. The following table outlines the fees paid or accrued to the auditors for the periods indicated:

Fees	Year ended December 31, 2008	Year ended December 31, 2007
Audit Fees	\$ 185,000 <sup>(1)</sup>	\$186,000
Audit – Related Fees <sup>(2)</sup>	\$ 63,000	\$ 76,000
Tax Fees <sup>(3)</sup>	\$ ,nil	\$ 1,000
All other Fees <sup>(4)</sup>	\$ 3,000	\$ 30,000
<b>TOTAL</b>	<b>\$ 251,000</b>	<b>\$293,000</b>

(1) Accrued for December 2008 Audit – BDO Dunwoody LLP.

(2) The fees related to quarterly reviews, reviews related to the filing of prospectuses by the Corporation and assistance in documenting certain corporate procedures.

(3) The tax fees include assistance in preparing tax returns for certain foreign subsidiaries and other general tax matters.

(4) Other fees relate to assistance provided in planning work related to the Corporation's obligations under MI52-109 and the CPAB fee.

### MATERIAL CONTRACTS

The only material contracts entered into by the Corporation during the recently completed financial year, or prior to the most recently completed financial year (but after January 1, 2002) that are still in effect, other than in the ordinary course of business, are as follows:

- the Debenture Indenture dated November 16, 2004 between the Corporation and Computershare Trust Company of Canada, described under “Description of Capital Structure – Description of the November 2004 Debentures”;
- the November 2004 Warrant Indenture dated November 16, 2004 between the Corporation and Computershare Trust Company of Canada, described under “Description of Capital Structure – Description of the Common Share Purchase Warrants Issued November 2004”;
- the 2006 Warrant Indenture dated June 20, 2006 between the Corporation and Computershare Trust Corporation of Canada, described under “Description of Capital Structure – Description of the Common Share Purchase Warrants Issued June 2006”;
- the Supplemental Warrant Indentures dated November 30, 2006 between the Corporation and Computershare Trust Company of Canada described under “Description of Capital Structure – Description of the Common Share Purchase Warrants Issued June 2006” and “—Description of the Common Share Purchase Warrants Issued November 2004”;
- the 2007 Warrant Indenture dated July 13, 2007 between the Corporation and Computershare Trust Corporation of Canada, described under “Description of Capital Structure – Description of the Common Share Purchase Warrants Issued July 2007”;
- the Supplemental Debenture Indentures dated January 1, 2007 and September 17, 2008, respectively, between the Corporation and Computershare Trust Company of Canada, described under “Description of Capital Structure – Description of the November 2004 Debentures”;

- the 2008 Rights Plan Agreement dated as of December 16, 1992 as amended and restated on May 1, 2008, between the Corporation and CIBC Mellon Trust Company of Canada, described under “Description of Capital Structure – Description of the Common Shares – Shareholder Rights Plan”; and,
- the Supplemental Warrant Indentures dated January 6, 2009 between the Corporation and Computershare Trust Company of Canada.

## EXPERTS

The Corporation’s auditor is BDO Dunwoody LLP, Chartered Accountants, 60 Columbia Way, Suite 400, Markham, Ontario L3R 0C9. BDO Dunwoody LLP has confirmed that it is independent with respect to the Corporation within the meaning of the Rules of Professional Conduct of the Institute of Chartered Accountants of Ontario. BDO provides tax, financial advisory, and other non-audit services to the Corporation and its subsidiaries. The Corporation’s Audit Committee has concluded that the provision of these non-audit services by BDO is compatible with BDO maintaining its independence.

## ADDITIONAL INFORMATION

Additional information regarding the Corporation can be found on the Internet at [www.sedar.com](http://www.sedar.com). Additional information on Nuvo, including directors’ and officers’ remuneration and indebtedness, principal holders of the Corporation’s securities, options to purchase securities and interests of insiders in material transactions is contained in the Corporation’s Management Information Circular dated March 26, 2008. Additional financial information is provided in the Corporation’s Consolidated Financial Statements and Notes to the Consolidated Financial Statements for the year ended December 31, 2008.

Copies of the Corporation’s Report to Shareholders for the year ended December 31, 2008, Management Information Circular and this AIF may be obtained upon request from the Corporation’s Investor Relations Department or on the Corporation’s web site: [www.nuvoresearch.com](http://www.nuvoresearch.com).

## GLOSSARY

<b>adjuvant</b>	Substance combined with another drug to enhance its immunogenicity (i.e. its ability to stimulate an immune response)
<b>AIDS</b>	Acquired Immune Deficiency Syndrome, the most severe manifestation of a wide spectrum of diseases caused by HIV.
<b>Akorn</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure – Corporate Structure – Akorn Pharmaceuticals Canada Limited”.
<b>analgesic</b>	A drug that relieves pain. Analgesics include non-prescription drugs such as acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, and those classified as controlled substances and available only by prescription.
<b>Approvable Letter</b>	Has the meaning ascribed thereto under “General Development of the Business – Products – Pennsaid®”.
<b>BfArM</b>	Germany’s Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte) is the German regulatory authority that oversees all clinical trials conducted in Germany.

<b>bioavailability</b>	The degree to which a drug or other substance becomes available to the target tissue after administration.
<b>Call Trading Condition</b>	The event whereby the closing price of the Common Shares traded on the TSX or, if not listed on the TSX, such other exchange or stock market on which the common shares may then be listed or quoted, equals or exceeds \$2.50 (subject to adjustment) for 20 consecutive Trading Days.
<b>Change of Control</b>	An occurrence involving (i) the acquisition, by any person or persons acting jointly or in concert in a single transaction or a series of related transactions, of voting control of or direction over 50.1% or more of the issued and outstanding Common Shares; (ii) the consolidation or merger of the Corporation with or into another person or the sale, assignment, transfer, lease or conveyance of all or substantially all, of the assets of the Corporation to another person, in each case, pursuant to a transaction where the common shares are converted into or exchanged for cash, securities or other property, other than: (A) any such transaction in which the outstanding Common Shares are converted into or exchanged for, voting securities or securities exchangeable at the option of the holder into voting securities of the surviving or transferee person constituting a majority of such voting securities; or (B) pursuant to a migratory merger effected solely for the purpose of changing the jurisdiction of incorporation of the Corporation.
<b>Clinical Trials</b>	The regulated process by which new drugs proceed after discovery through to acceptance for marketing to patients. The term most correctly refers to the period during which new compounds are tested in human subjects and encompasses the several phases as outlined under “Narrative Description of Business – Regulatory Environment”.
<b>CMC</b>	Chemistry, manufacturing and controls.
<b>Common Share</b>	Has the meaning ascribed thereto under “General Development of the Business – Recent Financings and Corporate Transactions”.
<b>COX</b>	Short form of cyclooxygenase, an enzyme in the cascade of biological reactions leading to the formation of prostaglandins, which cause both pain and inflammation.
<b>Conversion Price</b>	Has the meaning ascribed thereto under “General Development of the Business – Acquisitions”.
<b>CRO</b>	A Contract Research Organization is a company that conducts research on behalf of a pharmaceutical or biotechnology company.
<b>CTA – Clinical Trial Application</b>	Previously known as an Investigational New Drug application it must be filed and accepted by the TPD of Health Canada before human clinical trials may begin.
<b>cystitis</b>	Inflammation of the bladder.
<b>Debenture Trustee</b>	Has the meaning ascribed thereto under “Description of Capital Structure – Description of the Debentures – General”.
<b>DHCL</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure – Corporate Structure – Dimethaid Health Care Ltd.”
<b>Diclofenac sodium Dimethyl sulfoxide</b>	An NSAID that is the active pharmaceutical ingredient in Pennsaid®. Dimethyl sulfoxide is the molecular penetration enhancer used in Pennsaid®.
<b>Dioptric</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure

	– Corporate Structure – Akorn Pharmaceuticals Canada Limited”.
<b>DMgmt</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure – Corporate Structure – Dimethaid Management Inc.”
<b>DMI</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure – Corporate Structure – Dimethaid Manufacturing Inc.”
<b>Drug Master File</b>	A Drug Master File (DMF) is a submission to the FDA that may be used to provide confidential, detailed information about facilities, processes or articles employed in the manufacturing, processing, packaging, and storing of one or more human drugs. Neither law nor FDA regulations require the submission of a DMF. A DMF is submitted solely at the discretion of the holder. The DMF holder provides the written authorization to the FDA that allows the review of the Master File to support other regulatory applications. The information contained in a DMF may be used to support an Investigational New Drug Application (IND), a New Drug Application (NDA), an Abbreviated New Drug Application, another DMF, an Export Application or amendments to any of these. DMF's are generally created to allow a party other than the holder of the DMF to reference material without disclosing to that party the contents of the file.
<b>efficacy</b>	Capacity for producing a desired result or effect.
<b>FDA</b>	The United States Food and Drug Administration, an agency within the Department of Health and Human Services, the U.S. government's principal agency for protecting the health of all Americans, which is among other responsibilities charged with regulating pharmaceutical products in the United States.
<b>fqubed</b>	Has the meaning ascribed thereto under “Structure of Nuvo Research Inc. – Corporate Structure – fqubed, Inc.”
<b>GCP and GLP</b>	Good Clinical Practices and Good Laboratory Practices are standards for the conduct of clinical trials (including laboratory studies) the data from which are expected to be submitted to a regulatory agency such as the FDA. In the case of GLP these practices are defined by regulation. GCP have arisen from general accepted clinical practices within the industry.
<b>genotoxicity</b>	The amount of damage a genotoxin can cause to a DNA molecule. A genotoxin is a toxin (poisonous substance) which harms the body by damaging DNA molecules, causing mutations, tumours, or neoplasms.
<b>GMP</b>	Good Manufacturing Practices, i.e. guidelines established by the governments of various countries, including Canada and the United States, to be used as a standard in accordance with the World Health Organization's Certification Scheme on the quality of pharmaceutical products.
<b>HIV</b>	Human Immunodeficiency Virus, the virus that causes AIDS.
<b>HTE</b>	High throughput experimentation ("HTE") as pioneered by Nuvo enables more skin property measurements to be made, in a shorter time frame and usually at a reduced per-measurement cost. This is important because one cannot predict how a given drug will pass through the skin or the degree to which an MPE™ will affect its permeability. The Corporation accumulates such data using a number of proprietary HTE platforms, including INSIGHT™, STORM™ and TEMPEST™ as outlined in “Narrative Description of Business –

	Technology – Topical and Transdermal Drug Delivery – High Throughput Experimentation (“HTE”).
<b>Immune system</b>	The totality of organs involved in the body’s immunologic response to foreign antigens.
<b>IND</b>	Investigational New Drug application which must be filed and accepted by the FDA before human clinical trials may begin.
<b>Interest Obligation</b>	The Corporation’s obligation to pay interest on the November 2004 Debentures in accordance with the November 2004 Debenture Indenture.
<b>Interest Payment Date</b>	Has the meaning ascribed thereto under “Description of Capital Structure – Description of the November 2004 Debentures – General”.
<b>Investigator</b>	The individual from a clinic site who is ultimately in charge of a study, typically a physician.
<b>in vitro</b>	Literally in glass, as in a test tube. A test that is performed in vitro is one that is done in glass or plastic vessels in the laboratory.
<b>in vivo</b>	In the living body or organism. A test performed on a living organism.
<b>July 2007 Warrants</b>	Has the meaning ascribed thereto under “General Development of the Business – Recent Financings and Corporate Transactions”.
<b>June 2006 Warrants</b>	Has the meaning ascribed thereto under “General Development of the Business – Recent Financings and Corporate Transactions”.
<b>macrophage</b>	A type of white blood cell that coordinates aspects of the immune system.
<b>Maturity Date</b>	Has the meaning ascribed thereto under “Description of Capital Structure – Description of the November 2004 Debentures – Conversion Privilege”.
<b>metastatic tumour</b>	Cancer cells that develop in one body organ can spread to other body organs. Tumours formed by such cancer cells that spread (metastasize) to other organs are called metastatic tumours.
<b>MMPE™s</b>	Multiplexed molecular penetration enhancers are cocktails or combinations of MPE™s that modify the permeability of the stratum corneum.
<b>MPE™s</b>	Molecular penetration enhancers are molecules that interact with the molecules comprising the stratum corneum so as to modify its permeability.
<b>NDA</b>	New Drug Application, a document containing pre-clinical, clinical and chemistry, manufacturing and control data collected on a drug. An NDA is submitted to the FDA in order to obtain approval to market a prescription drug in the United States.
<b>neuropathic pain</b>	Neuropathic pain is a type of pain caused by injury to the nervous system. The injury can be to the central nervous system (brain and spinal cord) or the peripheral nervous system (nerves outside the brain and spinal cord). Neuropathic pain can occur after trauma or be associated with many diseases such as diabetes, shingles and cancer. Examples include post herpetic neuralgia, reflex sympathetic dystrophy/causalgia (nerve trauma), components of cancer pain, phantom limb pain, entrapment neuropathy (e.g., carpal tunnel syndrome), and peripheral neuropathy (widespread nerve damage).
<b>nociceptive pain</b>	Nociceptive pain is a type of pain associated with damage to the body. With this of pain the nociceptors, nerves which sense and respond to

parts of the body which suffer from damage, send signals of tissue irritation, impending injury, or actual injury are activated. They transmit pain signals (via the peripheral nerves as well as the spinal cord) to the brain. The pain is typically well localized, constant, and often with an aching or throbbing quality. Examples would include sprains, bone fractures, burns, bumps, bruises and inflammation from an infection or arthritis.

<b>November 2004 Debentures</b>	Has the meaning ascribed thereto under “General Development of the Business – Recent Financings and Corporate Transactions”.
<b>November 2004 Debenture Indenture</b>	Has the meaning ascribed thereto under “Risk Factors – Risks Relating to the Debentures”.
<b>November 2004 Warrants</b>	Has the meaning ascribed thereto under “Description of Capital Structure – Description of the Common Share Purchase Warrants Issued November 2004”.
<b>NSAID</b>	Non steroidal anti non-steroidal anti-inflammatory drug.
<b>OA</b>	Osteoarthritis has the meaning defined in “Glossary”.
<b>Ontario Action</b>	Has the meaning ascribed thereto under “General Development of the Business – Dispositions”.
<b>onychomycosis</b>	Onychomycosis is a fungal infection of the finger or toe nails.
<b>osteoarthritis</b>	Osteoarthritis (“OA”) is a type of arthritis that is caused by the breakdown and eventual loss of the cartilage of one or more joints. Cartilage is a connective tissue that serves as a "cushion" between the bones of the joints.
<b>OXO-K993</b>	A stabilized chlorite ion solution, the active ingredient used to produce WF10 and Oxoferin™ (of which the active pharmaceutical ingredient is referred to in the literature as TCDO, or tetrachlorodecaoxygen), as described under “Nuvo Research Inc. Structure – Corporate Structure – Dimethaid Immunology Inc.”.
<b>Paladin</b>	Has the meaning ascribed thereto under “Nuvo Research Inc. Structure – Corporate Structure – Dimethaid Health Care Ltd.”.
<b>p value</b>	A statistics term. A measure of probability that a difference in outcome between groups during an experiment happened by chance. For example, a p-value of .01 ( $p = .01$ ) means there is a 1 in 100 chance the result occurred by chance. The lower the p-value, the more likely it is that the difference between groups was caused by treatment.
<b>pharmacokinetics</b>	The action of drugs in the body over a period of time, including the processes of absorption, distribution, metabolism and excretion.
<b>placebo</b>	An inactive substance administered to a group of patients in a clinical study in order to form a control group against which the results obtained from patients receiving an active substance can be measured.
<b>pre-clinical studies</b>	Those studies generally completed prior to human clinical trials as outlined under “Narrative Description of Business – Regulatory Environment”.
<b>R&amp;D</b>	Research and development.
<b>Redemption Trading Condition</b>	The event whereby the closing price of the Common Shares traded on the TSX or, if not listed on the TSX, such other exchange or stock market on which the Common Shares may then be listed or quoted, during the 20 consecutive Trading Days ending five Trading Days immediately preceding the date on which notice of redemption is given,

	equals or exceeds 125% of the Conversion Price (as may be adjusted pursuant to the November 2004 Debenture Indenture).
<b>Squire</b>	Has the meaning ascribed thereto under “General Development of the Business – Products – Pennsaid®”.
<b>stratum corneum</b>	The stratum corneum refers to the outermost layer of the epidermis, which is itself the outer layer of the skin. The full name of the stratum corneum of the skin is the stratum corneum epidermidis.
<b>systemic</b>	Affecting the bodily system as a whole.
<b>topical delivery</b>	Delivery of a drug by application to the skin, usually with the objective of delivering the drug into or through the skin but without significant amounts reaching the bloodstream.
<b>toxicology</b>	Toxicology (also called Safety Pharmacology) is the study of a chemical compound to determine the levels at which death occurs.
<b>TPD</b>	Therapeutic Products Directorate. The division within Health Canada that reviews New Drug Submissions.
<b>Trading Day</b>	A day during which the TSX is open for trading and at least one board lot of the Common Shares has traded on the TSX.
<b>transdermal delivery</b>	Delivery of a drug through the skin, usually with the objective of realizing a systemic effect.
<b>Vianex</b>	Has the meaning ascribed thereto under “Narrative Description of the Business – Revenue Breakdown”.

## APPENDIX I – AUDIT COMMITTEE CHARTER

### AUDIT COMMITTEE CHARTER FOR NUVO RESEARCH INC. (the “Company”)

#### I. PURPOSE

The purpose of the Audit Committee (the “**Committee**”) is to assist the Board of Directors of Nuvo Research Inc. (the “**Board**”) in fulfilling its responsibilities of oversight and supervision of the accounting and financial reporting practices and procedures, the adequacy of internal accounting controls and procedures and the quality and integrity of the consolidated financial statements of Nuvo Research Inc. (the “Company”) and its affiliates. The Committee is also responsible for the audit process.

More specifically the purpose of the Committee is to satisfy itself that:

- A. The Company's annual financial statements are fairly presented in accordance with Canadian generally accepted accounting principles and to recommend to the Board whether the annual financial statements should be approved.
- B. The information contained in the Company's quarterly financial statements, annual report and other financial publications, such as management's discussion and analysis, is complete and accurate in all material respects and to recommend to the Board whether these materials should be approved.
- C. The Company has appropriate systems of internal control over the safeguarding of assets and financial reporting to ensure compliance with legal and regulatory requirements.
- D. The external audit functions have been effectively carried out and that any matter which the independent auditors wish to bring to the attention of the Board has been addressed. The Committee will also recommend to the Board the re-appointment or appointment of auditors and their remuneration.

#### II. COMPOSITION AND TERMS OF OFFICE

- A. Following each annual meeting of the Company, the Board shall appoint three or more directors to serve on the Committee. Such appointees shall not be officers or employees of either the Company or its affiliates. Each member of the Committee must be “Independent” as defined by Multilateral Instrument 52-110 and “Unrelated” according to the rules of the Toronto Stock Exchange (the “TSX”) from time to time, and free of any relationship that could, or could reasonably be perceived to, in the opinion of the Board, interfere with the exercise of independent judgment as a member of the Committee. All members of the Committee must be financially literate and be able to read and understand fundamental 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 Company's financial statements including the Company's balance sheet, income statement and cash flow statement, or develop that capability within a reasonable time after appointment.

- B. The chair of Committee shall be appointed by the Board and shall not be an officer or employee of the Company or its affiliates. The chair of the Committee shall be a “financial expert” having an understanding of GAAP and financial statements, internal controls and procedures for financial reporting and, if possible, shall have served as the principal financial officer for another business entity.
- C. Any member of the Committee may be removed or replaced at any time by the Board and shall cease to be a member upon ceasing to be a director of the Company. Each member of the Committee shall hold office until the close of the next annual meeting of the Company or until the member resigns or is replaced, whichever first occurs.
- D. The Committee will meet at least four times per year. The meetings will be scheduled to permit timely review of the interim and annual financial statements of the Company and its affiliates. Additional meetings may be held as deemed necessary by the chair of the Committee or as requested by any member of the Committee or by the external auditors.
- E. If all members consent, and proper notice has been given or waived, a member or members of the Committee may participate in a meeting of the Committee by means of such telephonic, electronic or other communication facilities as permit all persons participating in the meeting to communicate adequately with each other, and a member participating in such a meeting by any such means is deemed to be present at that meeting.
- F. A quorum for the transaction of business at all meetings of the Committee shall be a majority of the members of the Committee. Questions arising at any meeting shall be determined by a majority of votes of the members of the Committee present, and in case of an equality of votes the Chair of Committee shall have a second casting vote.
- G. The Committee may invite such directors, officers and employees of as it may see fit from time to time to attend meetings of the Committee and assist in the discussion and consideration of the business of the Committee, but without voting rights.
- H. The Committee shall keep regular minutes of proceedings and shall cause them to be recorded in books kept for that purpose, and shall report the same to the Board at such times as the Board may, from time to time, require.
- I. Supporting schedules and information reviewed by the Committee will be available for examination by any director upon request to the Secretary of the Committee.
- J. The Committee shall choose as its secretary such person as it deems appropriate.
- K. The external auditors shall be given notice of, and have the right to appear before and to be heard at, every meetings of the Committee, and shall appear before the Committee when requested to do so by the Committee.

### **III. DUTIES AND RESPONSIBILITIES**

Subject to the powers and duties of the Board, the Board hereby delegates to the Committee the following powers and duties to be performed by the Committee on behalf of and for the Board:

#### **A. Financial Reporting Control**

The Committee shall:

- (i) review reports from senior officers of the Company, outlining any significant changes in financial risks facing the Company;
- (ii) review the management letter of the external auditors and responses to suggestions made;
- (iii) annually review the Audit Committee Charter and the performance of the Committee itself;
- (iv) review any new appointments to senior positions of the Company or its affiliates, with financial reporting responsibilities; and,
- (v) obtain assurance the external auditors regarding the overall control environment and the adequacy of accounting system controls.

#### **B. Interim Financial Statements**

The Committee shall:

- (i) review interim financial statements with officers of the Company prior to their release and recommend their approval to the Board. This will include a detailed review of quarterly and year-to-date results; and
- (ii) review the Company's MD&A and press releases accompanying interim financial statements.

#### **C. Annual Financial Statements and Other Financial Information**

The Committee shall:

- (i) review any changes in accounting policies or financial reporting requirements that may affect the current year's financial statements;
- (ii) obtain summaries of significant transactions and other potentially difficult matters whose treatment in the annual financial statements merits advance consideration;
- (iii) obtain draft annual financial statements in advance of the Committee meeting and assess, on a preliminary basis, the reasonableness of the financial statements in light of the analyses provided by officers of the Company;
- (iv) review a summary provided by the Company's general counsel of the status of any material pending or threatened litigation, claims and assessments;
- (v) discuss the annual financial statements and the auditors' report thereon in detail with officers of the Company and its auditors;
- (vi) review the annual report and other annual financial reporting documents including management's discussion and analysis; (vii) provide to the Board a recommendation as to whether the annual financial statements should be approved;

- (vii) review insurance coverage including directors' and officers' liability coverage ; and
- (viii) review the Company's Annual Information Form ("AIF") and ensure compliance with FORM 52-110F1, audit committee information required in an AIF.

#### **D. External Audit Terms of Reference, Reports, Planning and Appointment**

The Committee shall:

- (i) ensure that the external auditor explicitly acknowledges that they are ultimately and directly accountable to the Board and the Committee as representatives of the shareholders;
- (ii) review the audit plan with the external auditors;
- (iii) specify its expectations of the external auditors, including the expected relationship between the external auditors and the Committee;
- (iv) discuss in private with the external auditors matters affecting the conduct of their audit and other corporate matters, including:
  - the quality (not only acceptability) of Canadian GAAP accounting principles;
  - the quality of internal controls;
  - the appropriateness of financial statement disclosures; and
  - any other matters the external auditors may wish to bring to the attention of the Committee.
- (v) recommend to the Board each year the retention or replacement of the external auditors. This process shall include establishment of criteria for and an ongoing assessment of the continued independence of the external auditor. If there is a plan to change auditors, review all issues related to the change and the steps planned for an orderly transition; and
- (vi) annually review and recommend for approval to the Board the terms of engagement and the remuneration of the external auditors.

#### **E. Other Matters**

The Committee shall:

- (i) pre-approve all non-audit services to be provided to the Company or its subsidiary entities by the issuer's external auditor.
- (ii) establish procedures for the receipt, retention and treatment of complaints received by the issuer regarding accounting, internal accounting controls, or auditing matters; and
- (iii) establish procedures for the confidential, anonymous submission by employees of the issuer of concerns regarding questionable accounting or auditing matters.

#### **IV. ACCOUNTABILITY**

- A. The Committee shall report to the Board at its next regular meeting all such action it has taken since the previous report.
- B. The Committee is empowered to investigate any activity of the Company and all employees are to co-operate as requested by the Committee. The Committee may retain persons having special expertise to assist it in fulfilling its responsibilities.
- C. The Committee is authorized to request the presence at any meeting, but without voting rights, of a representative from the external auditors, senior management, legal counsel or anyone else who could contribute substantively to the subject of the meeting and assist in the discussion and consideration of the business of the Committee, including directors, officers and employees of the Company.