ONCOLYTICS BIOTECH INC
Form 6-K
February 11, 2003

FORM 6K

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Report of Foreign Issuer

Pursuant to Rule 13a-16 or 15d-16 of
the Securities Exchange Act of 1934

For the month of **January, 2003**

Commission File Number **0-31062**

ONCOLYTICS BIOTECH INC.
(Translation of registrant s name into English)

Suite #210, 1167 Kensington Crescent N.W.
Calgary, Alberta Canada T2N 1X7
(Address of principal executive offices)

Indicate by check mark whether the registrant files or will file annual reports under cover Form 20-F or Form 40-F

Form 20-F X Form 40-F

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1): _____

Note: Regulation S-T Rule 101(b)(1) only permits the submission in paper of a Form 6-K if submitted solely to provide an attached annual report to security holders.

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7): _____

Note: Regulation S-T Rule 101(b)(7) only permits the submission in paper of a Form 6-K if submitted to furnish a report or other document that the registrant foreign private issuer must furnish and make public under the laws of the jurisdiction in which the registrant is incorporated, domiciled or legally organized (the registrant s home country), or under the rules of the home country exchange on which the registrant s securities are traded, as long as the report or other document is not a press release, is not required to be and has not been distributed to the registrant s security holders, and, if discussing a material event, has already been the subject of a Form 6-K submission or other Commission filing on EDGAR.

Indicate by check mark whether by furnishing the information contained in this Form, the registrant is also thereby furnishing the information to the Commission pursuant to rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes ___ No _[X]_

If Yes is marked, indicate below the file number assigned to the registrant in connection with Rule 12g3-2(b) 82___

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ONCOLYTICS BIOTECH INC.

Date: February 11, 2003

By: /s/ Doug Ball
Doug Ball, Chief Financial Officer

Note Regarding Forward Looking Statements

Certain statements in this document constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts, and include but are not limited to: the Company s financial projections and estimates and their underlying assumptions; statements regarding plans, objectives and expectations with respect to product research and development, clinical testing and commercial applications of the Company s technologies; the impact of regulatory requirements on the Company s products; the potential markets and applications for the Company s products; assumptions related to the pharmaceutical industry and the Company s competitors; and statements regarding future performance. Forward-looking statements generally, but not always, are identified by the words expects, anticipates, believes, intends, estimates, projects , potential , possible and similar expressions, or tha conditions will, may, could or should occur. Such forward-looking statements involve known and unknown risks, uncertainties and other factor which may cause the actual results, performance or achievements of Oncolytics Biotech Inc. (the Company), or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Such risks and uncertainties include, among others, the following:

the Company s primary potential product, REOLYSIN®, is in the research and development stage and is unlikely to be commercially available for a number of years, if at all;

the Company's success depends on its patents and its ability to protect its intellectual property rights;

the Company has a history of operating losses and future profitability is uncertain;

the Company anticipates that it will require additional capital to complete research, development and testing of its products and the availability of such capital on acceptable terms is uncertain;

the Company has limited manufacturing or marketing experience and will likely depend on strategic partners to commercialize its products;

the Company's success depends on the skills of its management and employees;

REOLYSIN® is in various stages of clinical trials for T2 prostate cancer and *malignant glioma*, and these clinical trials are long and expensive processes which will likely determine the commercial feasibility of REOLYSIN®;

the Company must obtain approval for its products from and meet the requirements of the Food and Drug Administration in the United States or the Health Protection Branch in Canada to commercially market its products;

the biotechnology industry is extremely competitive and the Company competes against companies with significantly greater financial and other resources;

the Company's products could fail or cause harm to patients which could subject the Company to product liability claims; and

other possible risks that are further described in the section entitled Risk Factors contained in the Company s annual report on Form 20-F for the year ended December 31, 2001, and the Company s quarterly reports on Form 6-K for the quarters ended March 31, 2002, June 30, 2002 and September 30, 2002, each filed with the United States Securities and Exchange Commission.

Such forward-looking statements are made as of the date of this report and management assumes no obligation to update such forward-looking statements. You are cautioned against placing undue reliance on forward-looking statements.

(**EXECUTIVE INFORMATIONAL OVERVIEW** IS PRESENTED VERTICALLY ALONG THE SIDE OF THIS PAGE 1 IN ORIGINAL)

Oncolytics Biotech Inc.
Suite 210, 1167 Kensington Crescent
Calgary, Alberta, Canada T2N 1X7
Phone: 403.670.7374
Fax: 403.283.0858
www.oncolyticsbiotech.com

January 23, 2003

A Unique Oncology Opportunity

Snapshot

Oncolytics Biotech Inc. was formed in 1998 to develop a naturally occurring, commonly found **virus** into a proprietary product called REOLYSIN® that does not harm normal cells but rather has the specificity to infect and kill approximately two-thirds of all human **cancer** cells.

Recent Financial Data

Ticker/Exchange	**ONCY/NASDAQ** **ONC/TSX**
Recent Price (01/22/03)	$ 1.26
52-Week Range	$2.95 - $0.91
Shares Outstanding	22.1 million
Avg 3-month vol. (NASDAQ)	16,545
Avg 3-month vol. (TSX)	58,500
EPS (mrq)	Cdn ($0.07)
Headquarters	Calgary, Canada

All amounts are in U.S. dollars, except where otherwise noted.

Key Points

The Company s approach is unique to a few other **oncology**-focused companies in that its technology, falling under a relatively new category of therapeutics called **virotherapy**, is based on the replication of the human **reovirus** (Respiratory Enteric Orphan virus). Normal healthy cells produce a certain **protein** that can kill the reovirus easily. In cancer cells with an activated **RAS pathway**, however, this protein is inactivated and thus cannot kill the reovirus.

The reovirus has been successfully studied as a cancer therapy in preclinical studies including animal models, tissue cultures, and human tumor specimens. Researchers have demonstrated that the reovirus is able to selectively kill human cancer cells **in vitro** and **in vivo** that are derived from many types of cancer, including breast, prostate, pancreatic, and brain tumors.

Phase I human clinical trial results have demonstrated no dose limiting toxicology-related issues with the administration of the reovirus to a broad range of cancers and that 11 of 18 late-stage cancer patients experienced tumor regression ranging from 32% to 100%.

Oncolytics Biotech has launched a T2 prostate cancer study (for cancer confined to the prostate gland) in up to 45 patients across Canada and has also launched a Phase I/II trial for **malignant glioma**, a very deadly form of brain cancer. For patients with **gliomas**, current treatment options are limited. In addition, the Company has stated that it expects to announce a third cancer target in the near future.

Oncolytics Biotech anticipates signing a partnership with a large pharmaceutical company prior to commencing late-stage testing of REOLYSIN®to continue its advancements in this area.

BOLD WORDS ARE REFERENCED IN GLOSSARY ON PAGES 29-32.

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Executive Overview

Oncolytics Biotech Inc. was formed in 1998 to develop the reovirus to treat a broad range of cancers. The Company s approach to treating cancer is unique to a few oncology-based companies in that its technology is based on the replication of a virus, specifically a formulation of the mammalian reovirus. The reovirus is a naturally occurring virus that is also an **oncolytic virus** (onco, meaning tumor or mass, and lytic, meaning **lysis** or destruction of cells) that selectively attacks and kills cancers, without affecting healthy cells and tissues.

Oncolytic viruses are believed to have a significantly higher **therapeutic index** than existing chemotherapies, meaning that oncolytic viruses are more specific in targeting and killing tumor cells while leaving healthy cells untouched. The Company believes, based on the preclinical and Phase I evidence, that the therapeutic index of the reovirus is at least 1,000:1. In fact, the Company has not seen any dose-limiting toxicity in any animal or human study conducted to date.

The **RAS gene** plays a pivotal role in cell biology. The gene acts as a controller a dispatcher that passes on biochemical signals to cells. The signals, in the form of proteins, tell the cell when to divide and when to stop dividing. Scientists say when the normal form of the RAS gene is

somehow damaged, whether through exposure to a carcinogen such as cigarette smoke or through a spontaneous biochemical mistake when the cell replicates, the protein ultimately manufactured by the defective, mutated form of the RAS gene is permanently switched on, thus defying signals to stop cell growth. The result is continuous cell division and tumor enlargement.

The molecular basis of the reovirus effect has been traced to **PKR**, a cellular enzyme involved in host cell **apoptosis** and growth control. Cancers that are RAS-activated compromise the activity of this protein, thus allowing the translation of reovirus proteins leading to the apoptotic death of the cancer cell. In a tumor cell with an activated RAS pathway, the reovirus is able to freely replicate and hence kill the host tumor cell. The cycle of infection, replication, and cell death is believed to be continual until there are no longer any tumor cells available carrying an activated RAS pathway. This process is illustrated in Figure 1. Approximately two-thirds of all cancers exhibit an activated RAS pathway, which leads Oncolytics Biotech to believe that the reovirus could become a successful cancer therapeutic for many human cancers.

Named for its Respiratory Enteric and Orphan features, the reovirus has been found widely in environmental sources, such as in sewage and in the water supply. Between 70% to 100% of the population has been exposed to the reovirus, typically without exhibiting any symptoms. We provide an image of the reovirus in Figure 2, on page 4.

Oncolytics Biotech is developing the reovirus under the trademark name of REOLYSIN® (pronounced REE-oh-LYE-sin) as a novel treatment for RAS-activated tumors and some cellular proliferative disorders. Reovirus could be thought of as a mild cold virus due to the symptoms that it may cause in the host; however, the reovirus is not **pathogenic**, meaning that there is no evidence that it causes disease.

Rather, it is a class of virus that is able to infect, multiply, and destroy human cells only if they possess an activated RAS pathway. As a result, REOLYSIN® could become a potential local and systemic therapeutic for up to two-thirds of all human cancers, including, but not limited to, malignant glioma (brain cancer), pancreatic cancer, colon cancer, and some lung cancers.

To date, the reovirus has demonstrated therapeutic potential in animal models, tissue cultures, and human tissue specimens. While a number of studies continue, which have yet to be published, there are a variety of published studies that address the three elements that the Company believes could be key to the success of the reovirus clinical trials. These include (1) demonstration of efficacy or potency; (2) evaluation of safety; and (3) the outcome of immune system interaction with the reovirus.

Final results of a Phase I human trial, which evaluated the dose-limiting toxicity and maximum tolerated dose of

REOLYSIN®, were announced in March 2002. The secondary endpoint was to document tumor regression. Data showed that *none* of the patients receiving REOLYSIN® experienced any serious adverse events related to the reovirus, nor were there any dose-limiting toxicities detected in any of the patients. Tumor responses were measured at both the treated lesion as well as remote tumor sites. Evidence of viral activity was detected in 11 of 18 patients (61%), with the tumor regression ranging from 32% to 100%. Viral activity is defined as a transitory or lasting tumor regression of at least 30% measured in two dimensions against the tumor size prior to injection on the first day of treatment.

Following the success of the Phase I trial, Oncolytics Biotech announced in April 2002 a human clinical trial of REOLYSIN® for T2 prostate cancer in up to 45 patients and in July 2002 a Phase I/II trial for recurrent malignant glioma, which is the most aggressive form of brain cancer, in up to 38 patients. The Company also plans to pursue trials for malignant glioma in the U.S. and additional clinical trials for other cancer indications in the U.S. and Canada, including a systemic application.

In addition to its proprietary technology, Oncolytics Biotech recently acquired minority positions in two other Canadian biopharmaceutical companies, BCY LifeSciences Inc., which has license rights to technologies to treat certain diseases of the respiratory tract, including cystic fibrosis, and Transition Therapeutics Inc., which is developing innovative therapeutics specifically for the treatment of multiple sclerosis, diabetes, and restenosis.

Headquartered in Calgary, Alberta, Canada, Oncolytics Biotech employs nine people, including four involved at the clinical trial level. Additionally, the company engages approximately 40-50 individuals on a consulting or contract basis who are FTEs (full-time equivalents) in the areas of clinical development and regulatory affairs, patent protection, and clinical trial management.

Growth Strategy

Oncolytics Biotech is focused on the research and development of REOLYSIN® for the multi-billion dollar human cancer market. The National Institutes of Health estimates that the overall costs for cancer in 2001 were $156.7 billion: $56.4 billion for direct medical costs (total of all heath expenditures), $15.6 billion for indirect morbidity costs (cost of lost productivity due to illness), and $84.7 billion for indirect mortality costs (cost of lost productivity due to premature death). REOLYSIN® is based on the successful demonstration of the oncolytic capabilities of the mammalian reovirus in both tissue culture and animal models, as well as a successful Phase I human trial. There have been a variety of preclinical studies that have demonstrated that the reovirus is highly effective in killing cancer cells, with either minimal or no side effects.

The Company has chosen to initially focus on developing REOLYSIN® for malignant glioma, since this is the most aggressive and deadly form of brain cancer with no truly effective treatment alternatives. This indication is undergoing a Phase I/II trial. Additionally, the Company is testing the effectiveness of REOLYSIN® for T2 prostate cancer. The clinical strategy is to develop REOLYSIN® and have it approved for sale as a cancer therapeutic in the shortest period of time. The prostate trial is a technical study that is expected to yield information about REOLYSIN® s ability to kill cancer cells within the prostate gland. After injection, the prostate glands are removed three weeks later as part of

standard therapy. The prostate glands can then be examined for evidence of viral activity. Patients with gliomas have a limited life expectancy, meaning that the Company should be able to quickly measure REOLYSIN® s safety and efficacy in this type of cancer. **Systemic** trials for a yet-to-be-determined cancer indication are expected to commence sometime early next year at several well-known clinical centers.

Because Oncolytics Biotech is a small biotechnology company, the Company has stated that it expects to initiate a strategic partnership prior to the start of any large-scale Phase III trial for the critical market approval submissions. Additionally, by having a more substantive marketing partner, Oncolytics Biotech believes this will facilitate the support of key specialists in the applicable field of medicine, affording its product the maximum possible exposure.

Intellectual Property

Since Oncolytics Biotech is a relatively early-stage biotechnology company, protection of its intellectual property is key to the ongoing viability of its business. It is also crucial to increasing its value to potential strategic partners. Additionally, since REOLYSIN® is the **wild-type** reovirus, serotype 3, which is naturally occurring, the Company may not be able to claim composition of matter patents for the drug. Rather, it has focused on use and process patents.

To date, the Company now has five U.S. patents and is awaiting approval of several more. Additionally, it has one European patent. The Company currently has greater than 100 patent applications pending worldwide for the use of the reovirus as a cancer therapeutic, methods of manufacturing, and more.

Officers and Directors

Key Management

Brad G. Thompson, Ph.D., Chairman, President, and Chief Executive Officer

Dr. Thompson has provided leadership to various organizations within the biotechnology sector for almost 20 years. Prior to his role with Oncolytics Biotech, he held a number of senior executive positions with SYNSORB Biotech from 1994 to 1999. From 1983 to 1994, Dr. Thompson worked in a senior role at The Alberta Research Council. Dr. Thompson sits on the boards of five publicly traded companies. He received his Ph.D. from the University of Western Ontario in the Department of Microbiology and Immunology.

Doug Ball, CA, Chief Financial Officer

Mr. Ball is a senior executive with more than 25 years of experience in accounting, finance, and developing and implementing effective business strategies. He is responsible for the financial affairs of Oncolytics Biotech and provides financial and commercial input into the strategic direction of the Company. Prior to joining Oncolytics Biotech, Mr. Ball held a variety of senior positions with organizations including

SYNSORB Biotech, Canadian Airlines and Canadian Regional Airlines, Time Air, and the Nu-West Group.

George Gill, M.D., Senior Vice President, Clinical and Regulatory Affairs

Dr. Gill has more than 30 years of senior-level experience in clinical research and regulatory affairs, and has supported the advancement of more than 20 products, including 11 cancer products, through the regulatory approval process in the United States, Canada, and Europe. Prior to joining Oncolytics Biotech, Dr. Gill held top positions with several major pharmaceutical companies including ICI Pharmaceuticals (now AstraZeneca), The Bristol-Myers Company (now Bristol-Myers Squibb Company), and Hoffman-La Roche. Dr. Gill holds a B.S. in chemistry from Dickinson College in Pennsylvania and an M.D. from the School of Medicine at the University of Pennsylvania.

Matt Coffey, Ph.D., Vice President, Product Development

A co-founder of Oncolytics Biotech, Dr. Coffey s current responsibilities include managing the clinical trial program and protecting Oncolytics Biotech s intellectual property position. Prior to joining Oncolytics Biotech, Dr. Coffey completed his doctorate degree in oncology at the University of Calgary with a focus on the oncolytic capabilities of the reovirus. The results of his research have been published in several respected scientific journals, including *Science*, *Human Gene Therapy*, and *The EMBO Journal*.

Wayne Schnarr, Ph.D, Vice President, Corporate Development

Dr. Schnarr has over 25 years of experience in the pharmaceutical and financial industries and has been involved with cGMP manufacturing, corporate partnerships, mergers, and public market financings. He has held senior management positions and has been a director for a number of public and private biotechnology companies, of which Oncolytics Biotech is the third with a cancer product development program. He obtained his Ph.D. in chemistry from Queen s University and his MBA from York University.

Board Members

William A. Cochrane, OC, M.D.

Dr. Cochrane, most recently appointed to Oncolytics Biotech s Board of Directors, is currently the Chairman of Stressgen Biotechnologies Corporation, President of W.A. Cochrane & Associates Inc., Chairman of UTI at the University of Calgary, and serves on the boards of a number of Canadian and American companies. Previously, Dr. Cochrane was the CEO and Chairman of Connaught Laboratories Ltd. He has also served as the Deputy Minister of Health Services for the Province of Alberta, and President and Vice-Chancellor, and Dean of Medicine at the University of Calgary. He has served on the boards of MDS Capital Corp., Connaught Laboratories Ltd., Monsanto Canada Inc., and Fluor/Daniel Canada Inc. Dr. Cochrane is an Officer of the Order of Canada and a 2002 recipient of the Queens Golden Jubilee Medal for his

many contributions to Canada. He received his M.D. from the University of Toronto.

George Masters

Mr. Masters is Chairman of the Board of SignalGene since April 2001 and Director since September 2000. He is also Chairman of the Board of BioCatalyst Yorkton since December 1996 and Vice Chairman of Hemosol since 1992. Mr. Masters currently holds directorships in a number of biotechnology companies and has spent decades working in the international healthcare and biotechnology industries, including 20 years with Warner-Lambert where his last position was President of the worldwide diagnostics business.

Antoine Noujaim, Ph.D.

Dr. Noujaim is Chairman and Chief Executive Officer of Virexx Research Inc. since August 2002 (which was previously Novolytic). Prior to this, he was Chairman of the Board of AltaRex Inc., a public biopharmaceutical company since 1998. Dr. Noujaim was President and Chief Executive Officer of AltaRex Corp., from November 1995 to February 1998. From 1994 to 1995, he was the President of Biomira Research Inc., a division of Biomira Inc. (a public biopharmaceutical company) and Senior Vice President of the Immunoconjugate Division of Biomira Inc. from 1989 to November 1995. Dr. Noujaim also served as a Director of Biomira Inc. from 1985 to 1995. Dr. Noujaim received his B.Sc. in Pharmaceutical Chemistry from Cairo University in 1958. He obtained an M.Sc. and Ph.D. in Bionucleonics as a Fulbright scholar from Purdue University in 1963 and 1965, respectively.

Robert B. Schultz, F.C.A.

Mr. Schultz is Chairman of Rockwater Capital Corporation. He was formerly Chairman and CEO of Merrill Lynch Canada, a role he assumed in 1998 after orchestrating the merger of Midland Walwyn with Merrill Lynch. Mr. Schultz is the former Chairman and CEO of Midland Walwyn and has held a variety of other senior positions in companies including Wood Gundy, Davidson & Partners, and Merrill Lynch Royal Securities. Mr. Schultz has also served on the Board of Directors of the Investment Dealers Association of Canada (IDA) from 1991 to 1996 and was Chairman from 1994 to 1995. He is currently a director or advisor to several other private and public companies.

Fred A. Stewart, LL.B., Q.C.

Mr. Stewart is the President of Fred Stewart & Associates Inc., consulting primarily to clients in the advanced technologies sector since 1993. Mr. Stewart served as a member of the Alberta Legislative Assembly from 1986 to 1993, with responsibilities as Minister of Technology, Research, and Telecommunications and Government House Leader. Before this period of public service, Mr. Stewart was a founding partner of a Calgary law firm, where he practiced primarily corporate and commercial law for over 20 years. In addition to his consulting practice, Mr. Stewart serves in a number of capacities for various organizations in Alberta s technology sector. Mr. Stewart also serves on the boards of several Alberta-based technology corporations. In 1999, Mr. Stewart was honored as the recipient of a special award from the Alberta Science and Technology Foundation for his contribution to Alberta s advanced technology community.

Core Story

Cancer Overview

Cancer is a family of diseases in which cells grow and spread uncontrollably throughout the body, disrupting the balance between new cell growth and old cell death. In a healthy person, the multiplication of cells is carefully regulated, such as for babies and children, where cell multiplication exceeds cell death and a person grows in size. In an adult, cell multiplication and cell death achieve a steady state because while some cells are continuously dying and being replaced, such as intestinal cells, white blood cells, and red blood cells, others have negligible replacements, such as brain cells.

Because abnormal cells are originally produced within the body, the body does not recognize them as foreign and, therefore, does not respond through the typical immune response of destroying the foreign substance. Cancer cells that escape the body s immune system can spread throughout the body in a variety of ways, invading and destroying healthy human tissue, which can eventually cause death. Cancer is composed of either solid tumors or blood-borne cancerous cells, which, over time, tend to spread to other tissues and organs of the body (**metastasis**).

Cancer can occur from **gene** mutations. Sources of mutations can include toxin exposure (smoking, asbestos, etc.), heredity, sun exposure, and infection exposure (such as for the human papillomavirus). It can take many years for these mutations to accumulate, which is why cancer is usually associated with older people. This is supported by the fact that greater than three-quarters of all cancers are diagnosed in people age 55 and older.

Typically, cancer that is detected early on in its progression has the best prognosis. In this scenario, if the cancer has not spread to other organs and tissues, surgical removal of the tumor can be effective. However, cancer that is detected at a later stage frequently has the worst prognosis, as it has often already spread to the organs and tissues within the body.

This is not to say that all cancers, when detected early, can be cured through surgery. In many situations, the cancer has spread or surgery cannot remove the entire tumor from the body, thus making the patient s prognosis bleak. In such cases, even if the bulk of the tumor is removed, the prognosis may be poor due to the spread of undetectable cancer cells (**micrometastasis**). Thus, if the cancer is not discovered early enough, it may have already entered the blood or lymphatic system and may have established new tumors at other sites. Tumors formed at these new sites are extremely difficult to treat through current therapies.

Cancer Statistics

While remarkable strides have been made in understanding cancer biology and improving upon current cancer therapies, the combined death rate from all cancers has not changed dramatically in 25 years, though survival rates have improved as more effective treatments have come to market. While the cause of many cancers is still unknown, what is known is that occurrence increases with age and multiple risk factors have been identified. Triggers that are a common link to cancer development include chemicals, radiation, and certain viruses (such as the human papillomavirus, which can lead to cervical cancer), as well as specific internal factors, such as hormones, immune conditions, and inherited mutations.

The American Cancer Society estimates that there are currently 8.9 million people in North America with a history of cancer, approximately 1.3 million who are expected to be diagnosed with cancer this year, and more than half a million people expected to die from cancer this year. Specifically, in the U.S., greater then 555,000 people are predicted to die from cancer this year, or more than 1,500 people per day. After cardiovascular diseases, cancer remains the most common cause of death, with about one out of every four U.S. deaths linked to this disease. The relative lifetime risk of a male developing cancer is one in two; for women the risk is one in three. Additionally, The National Cancer Institute (NCI) anticipates that cancer may exceed cardiovascular disease as the leading cause of death in the next decade.

Lung cancer leads this category in terms of deaths reported, with 155,000 U.S. deaths forecasted for this year. This is followed by colon and rectal cancers, which is forecast to cause 57,000 deaths; liver cancer, which is forecast to cause 54,000 deaths; and breast cancer, which is forecast to cause 40,000 deaths. Table 1 (on page 10) provides a comprehensive list of the estimated new cases for each leading category of cancer, as well as the associated deaths (categorized by gender). The anti-cancer treatment market represents a mere 5% of the global pharmaceutical market, despite the fact that it is the second leading cause of death in developed countries, accounting for approximately one-quarter of all mortalities. The only higher incidence of disease is cardiovascular, with a 33% mortality rate, according to the American Cancer Society. Important to point out is that a lack of health insurance and other barriers prevent many Americans from receiving optimal healthcare treatment once diagnosed with cancer.

Current Cancer Treatments

While surgery continues to be the most effective first-line therapy for certain cancers that are considered operable, other forms of cancer that are systemic or have metastasized to become inoperable and are considered difficult to treat require alternative approaches. The past several decades have brought about exciting new developments in the area of cancer research. In the past six years, there have been nearly 80 Food and Drug Administration (FDA)-approved, cancer-related medications or new uses of already available drugs that treat a variety of cancers, according to the FDA. Additionally, doors have opened for new and better ways to halt or reverse the cancer process. The need, however, is still critical to bring about more effective treatments that can provide cancer patients with a longer and improved quality of life compared to current treatments. Thus, research and development within the area of cancer research remains as strong as ever.

According to The Pharmaceutical Researchers and Manufacturers of America (PhRMA), there are currently greater than 400 companies investigating new products and/or approaches for treating/curing cancer and approximately 450 products in clinical trials, of which 80 are in Phase III. These 450 include 68 treatments for lung cancer, the leading cause of cancer death in the U.S.; 59 for breast cancer, which strikes one out of every ten American women; 55 for colon cancer, which has the third highest incidence of any cancer site for American men; 52 for skin cancers (including melanoma, the deadliest form, whose incidence has grown 4% a year since the 1970 s); and 52 for prostate cancer, which kills 37,000 men a year. Just under half of the products in clinical trials are based on biological agents such as **vaccines**, **monoclonal antibodies**, cytokines, gene therapy based on cytokines, and protein conjugates. Additionally, there are more than 1,000 products undergoing preclinical testing.

We outline some of the leading areas of research underway for cancer therapy. These areas are in addition to the four major treatment options most commonly employed surgery, radiation, chemotherapy, and biologic therapies. Still without a cure, doctors must design individual therapies using the options currently available based on (1) the type of cancer, (2) a patient s age, (3) a patient s particular health status, and (4) a patient s wishes.

Following the discussion below of the major areas at the forefront of cancer research, we detail Oncolytics Biotech s technology on pages 21-24, describing how its approach is unique from these other areas of research. We then describe where the Company is in its development stage for bringing REOYLSIN® to market and for which cancer indications.

Targeted Approaches

While the most commonly employed cancer treatments still generally include surgery, chemotherapy, and/or radiation, which are successful at treating *some* cancers, each of these treatments carry limitations and/or serious side effects. These limitations include not always killing every cancer cell, or in the process of killing cancer cells, killing normal cells as well. These treatments can also make patients extremely sick, to the point where some patients cannot tolerate further treatment. Consequently, scientists continue to pursue better ways to target therapies directly to the tumor, while still protecting healthy cells. Some such strategies, referred to as targeted approaches, include:

attacking the unique characteristics of the cancer cells. With a better understanding of how cancer cells grow and spread, researchers are beginning to focus on various ways to alter this process.

making a tumor more susceptible to a cancer drug . Since drugs can now more precisely target cancer cells, higher doses can sometimes be administered.

reducing side effects of cancer drugs. Newer drugs are designed to attack only the cancer cells, without harming healthy cells. They are, therefore, less likely to cause side effects such as hair loss, nausea, and diarrhea.

Some of the aforementioned approaches may stop the growth of existing tumors and/or prevent new tumors from developing, but they may not necessarily remove the cancer altogether. In the future, certain cancers may also be managed over longer durations with regular drug therapies.

This manner of controlling the disease could become similar to that of other chronic diseases, such as heart disease or diabetes.

Gene Therapies

Part of a new cancer treatment strategy includes changing the genes that affect how cancers grow. Scientists are testing different ways of doing this, including:

altering cells to boost their cancer-fighting ability. In this situation, scientists take cells from a patient and change them to create a healthy copy of the missing or flawed gene. These altered cells are then injected back into the patient where they are better able to attack the cancer.

injecting a tumor with genes that will make it more susceptible to chemotherapy or other therapies.

altering the genes of cancer cells so that the patient s own immune system will fight against them.

Immune System Boosters

Scientists use various therapies to repair, stimulate, or enhance the fighting ability of the immune system. There are a number of agents under development that act along with the immune system to help fight cancer, including:

*interferons.*These naturally occurring, cancer-killing substances defend against viruses, bacteria, and other agents that cause disease.

interleukins. These cancer-killing substances occur naturally, though they can also be created in the laboratory.

tumor necrosis factors (TNF). These substances target and kill cancer cells and disrupt blood vessels within the tumor.

monoclonal antibodies. These antibodies target specific parts of cancer cells.

Vaccines

Cancer vaccines may be able to prevent or treat cancer in different parts of the immune system. Some attempt to induce an **antibody** response to prevent cancer in the first place; others activate an arm of the immune system to kill existing cancerous cells. Either way, a cancer vaccine is designed to get a body s immune system to attack foreign materials within the body. The body then recognizes foreign material by introducing a small amount of the target material (the **antigen**). To make these targets for cancer vaccines, scientists take parts of tumor cells (i.e., proteins or **enzymes**) that are unique to those cells and make them harmless. The vaccine is then injected into the body.

Injectable vaccines are currently the focus of research for many companies and organizations; however, researchers are also looking at the possibility of developing a vaccine that could be swallowed, inhaled, or otherwise introduced into the body. Should these new cancer vaccines prove successful, they could eventually become part of standard cancer therapy. They also could be used in combination with already available treatments, such as chemotherapy. Additionally, they could be used for patients who have had cancer before and are at high risk for their cancer returning. Specifically, vaccines have shown success in treating melanoma (skin cancer), colorectal cancer, breast cancer, prostate cancer, and lymphoma.

Blocking a Tumor s Blood Supply (Antiangiogenesis Drugs)

A tumor needs a constant supply of blood and nutrients to grow. Its ability to produce new blood vessels is called **angiogenesis**. Scientists are studying ways to cut off the tumor s blood supply, an approach they believe will essentially starve the tumor to death. A number of drugs are under development that may block angiogenesis. These agents are called angiogenesis inhibitors, or **antiangiogenesis** drugs.

Hormone Therapy

Some cancers are very sensitive to hormones, such as certain breast cancers and prostate cancer. Developments are underway to deliver agents that suppress estrogen in women with breast cancer and other agents that block **androgens** in men with prostate cancer.

Killing Tumors Using Light

While surgery has been successfully used for many years to remove cancerous tumors, not all cancers can be surgically removed. Even when they can be removed, some cancerous cells may be missed and/or left in the body. Researchers are experimenting with new methods that can be used along with surgery. One of the most exciting developments is the use of light. For this type of treatment, a light-sensitive drug is given to patients before they undergo surgery. Following surgery, a laser beam is directed at the tumor site where the drug has accumulated, triggering the drug to release chemicals that kill any cancer cells that were missed, without affecting any healthy cells. This technique has been used in early stages of bladder and esophageal cancers. It is now being tested in brain cancer.

Other New Interventions

Researchers are also testing the use of heat, such as microwave energy, to help kill cancer cells. Additionally, they are studying ways to use cold substances, such as alcohol, that might freeze or otherwise kill cancer cells. Another new area is the use of magnetic particles to draw cancer-killing agents into tumors. Many of these approaches are years away from being available; however, this research creates opportunities for the development of new classes of cancer treatments. It also provides hope that many more cancers can be successfully treated and, more importantly, managed in the future by either a single drug or combination of therapies.

Virotherapy

The vast potential for viruses as a magic bullet against cancer is currently driving developments within an area called virotherapy. These oncolytic viruses, or cancer-killing viruses, are believed to be an improvement over current cancer therapies. Common cancer treatments, such as chemotherapy and radiation, typically carry significant side effects due to their toxicity to both normal cells and tumor cells. *Virotherapy is unique among other cancer therapies since it seeks to harness the natural properties of viruses to aid in the fight against cancer while at the same time maintaining normal healthy cell function.*

Cancer s ability to become resistant to conventional therapies over time has propelled research in this area. Traditional viral therapy approaches have focused primarily on the insertion of genes encoded with suicide proteins, or tumor suppressor proteins (cytokines). The impact of these alterations often compromises the ability of the altered viruses to replicate. Restricting the ability to replicate, however, has limited the efficacy since this restricts the number of cells to which the altered viruses are delivered. Consequently, replication-competent viruses are being investigated, which could lead to lysis of more tumor cells. Oncolytics Biotech is one of a group of organizations that believes that virotherapy may be able to demonstrate improved efficacy in destroying tumor cells compared to other methods of treatment, with superior safety due to its limited impact on normal cells.

Replication-competent viruses such as the reovirus work in the following way. Once the virus infects the tumor cell, in which cancer has compromised the cell s natural defense mechanisms, the virus starts to

replicate. The virus replicates until finally the tumor cell bursts. Thousands of newly created viruses are then spread to neighboring cancer cells to continue this cycle. It is important to clarify that all oncolytic viruses are intended to replicate only in cancer cells and enter normal tissues without causing them harm. Once all the susceptible tumor cells are eradicated, the oncolytic virus no longer has the ability to replicate and the immune system clears it from the body.

Approximately one-half of human cancers are associated with mutations in the **p53 tumor suppressor** gene. This gene normally suppresses tumors, though in most cancer patients it is defective. In addition, mutations in the RAS **oncogene** are associated with approximately 30% of human tumors, approximately two-thirds including upstream RAS mutations, and an even higher percentage of malignant cancers. Two of the viruses that are being developed as cancer killers are targeting the p53 and the RAS genes. **Adenovirus vectors** are being designed to infect and kill cells lacking p53, while REOLYSIN® infects and kills cancer cells with an activated RAS pathway.

Intratumoral versus Intravenous Virotherapy

Research efforts are in progress at numerous organizations throughout the world to thoroughly evaluate the safety and efficacy of oncolytic virus therapies. The majority of studies are utilizing **intratumoral** delivery of the oncolytic virus therapies. Direct administration into the tumor allows the oncolytic virus immediate access to the cancer cells in which they replicate and ultimately destroy.

Additional studies are also being conducted to determine the safety and efficacy of **intravenous** administration of oncolytic virus therapy. While intravenous administration holds the promise of providing systemic treatment and targeting cells that have spread from the primary tumor source, researchers are faced with the challenge of maintaining therapeutic levels of the virus in the presence of the immune system, which intrinsically seeks to rid viruses from the body. Intravenously administered oncolytic virus therapy must, therefore, overcome pre-existing antibodies in order to achieve a therapeutic effect if they are present at a level that would antagonize effectiveness. Alternatively, research is being conducted to determine a way to modulate the immune response, thus allowing the virus time to reach the primary tumor source as well as target cancer cells that have spread throughout the body.

Engineered versus Non-Engineered Virotherapy

Research is also underway using both non-engineered and engineered viruses to evaluate their use in the fight against multiple types of cancer. Non-engineered viruses are naturally occurring viruses that innately, preferentially target and replicate in certain types of tumor cells. Some non-engineered viruses include the Newcastle Disease virus (NDV) and the reovirus. Each of these is described on pages 15-19. Conversely, engineered viruses do not innately, selectively target and replicate in cancer cells. Scientists must genetically modify (engineer) the virus to selectively target and/or replicate within specific types of cancer cells.

Viruses Under Development for Oncolytic Applications

Within the area of virotherapy research and in addition to Oncolytics Biotech s efforts, approximately one half-dozen publicly traded biotechnology companies throughout North America are developing various viruses as cancer therapeutics. These companies include Cell Genesys Inc., Geron Corp., Introgen Therapeutics Inc., Medigene AG, Onyx Pharmaceuticals Inc., and Transgene S.A. Additionally, various teaching facilities and organizations are researching and/or developing therapies that fall within the area of virotherapy.

Table 2 provides a snapshot of selected publicly traded companies involved in virotherapy research, including the company s stock information, the nature of its research, the stage of development, and key financial information. We also describe each of these technologies in the subsequent section, noting that this list is not meant to be all-inclusive but rather is meant to provide an overview of those technologies that Oncolytics Biotech and The Investor Relations Group consider to be within a similar realm of Oncolytics Biotech s technology mainly the adenovirus, Herpes Simplex Virus (HSV), Newcastle Disease virus, Parvovirus, Poliovirus, Poxvirus, Retroviruses, and Vesicular stomatitis virus. We begin with the adenovirus since a great deal of research is taking place within this area.

ADENOVIRUS

Cell Genesys, Geron, Introgen, Onyx, and Transgene are each attempting to use the adenovirus as a potential cancer therapeutic. The result of an adenovirus infection is cold-like symptoms; a normal infection from this virus includes acute mucous membrane infections of the upper respiratory tract, eyes, and regional lymph nodes. In these viruses, tumor specificity is lacking and extensive work must be performed in order to modify these viruses to improve their infectivity, apoptotic ability, and lytic ability. Modifications include expression of **Prostate Specific Antigen** (PSA), knockout of E1B (killing cells that lack functional p53), expressing the human p53 gene, and expressing interferon-gamma. Cancers being targeted for potential treatment with the adenovirus include prostate, head and neck, pancreatic, liver, ovarian, non-small cell lung cancer, and melanoma. We describe the efforts below of each of the companies developing the adenovirus as a potential cancer therapeutic. Figure 3 (page 16) illustrates the structure of an adenovirus.

Cell Genesys is conducting clinical trials on multiple types of cancer utilizing its GVAX® cancer vaccines and oncolytic virus therapies. In September 2002, the company updated long-term survival data from its initial Phase II multi-center trial of the GVAX® prostate cancer vaccine in patients with advance-stage, hormone refractory prostate cancer. In the 34-patient study, 5 of 10 (50%) patients receiving the higher of 2 dose levels of the vaccine remained alive for 2.5 years after treatment (median survival = 31 months). Of the 24 patients receiving the lower dose of the vaccine, 7 of 22 patients (32%) remained alive for 2.5 years after treatment (median survival = 22 months), and 2 were lost to follow-up. Based on these encouraging data, Cell Genesys has stated that it expects to initiate a Phase III clinical trial by mid-2003.

Also, in June 2002, Cell Genesys reported updated data from its Phase II trial of advance- and early-stage patients that evaluated a GVAX® lung cancer vaccine prepared completely from the patient s own tumor cells. Of the 33 advance-stage patients, most of whom had failed prior chemotherapy and/or radiation therapy, 3 patients (9%) experienced durable complete responses, which were maintained for at least 16 months. Two of these patients were noted to have a sub-type of lung cancer known as bronchoalveolar carcinoma (BAC). Based on these data, Cell Genesys expects to initiate two Phase II clinical trials of patients with BAC by early 2003 one of which will be funded by the National Cancer Institute. A Phase III trial in all types of non-small cell lung cancer is also targeted to begin in late 2003.

Geron Corporation sproduct development programs are based on three patented core technologies: **telomerase**, human embryonic stem cells, and nuclear transfer. The company is developing customized adenoviruses that will infect and kill cancer cells that express telomerase and not infect and kill normal cells that do not express telomerase. To pursue this goal, Geron has cloned the region of the **hTERT** gene, called the promoter sequence, which is responsible for turning on or off the activity of telomerase in a cell. The company has shown that this promoter is turned on in telomerase-positive cancer cells and is turned off in most normal cells.

Geron has data to indicate that when tumor cells are infected with the adenovirus that contains the hTERT promoter, the virus replicates within the cancer cells and causes the rupture and death of the tumor cells. When these same adenoviruses containing the hTERT promoter infect normal **somatic cells**, there is no similar effect on the cells. Geron has granted a non-exclusive license to Genetic Therapy Inc. (GTI), a subsidiary of Novartis AG, to use its telomerase promoter technology in oncolytic virus products.

Introgen Therapeuticsis involved in treating patients with its lead product candidate, ADVEXIN®, an adenoviral p53 gene therapy, in approximately 20 ongoing and/or completed Phase I, II, and III clinical trials worldwide. Introgen s second product candidate, INGN 241, is in Phase II clinical development. Introgen s current and expected clinical trials evaluate the company s products both alone and in combination with conventional treatments, chemotherapy, radiation, and surgery.

Onyx Pharmaceuticalsis developing a mouthwash that is a saline solution containing a virus genetically engineered to attack cells as they become cancerous. Cells in the mouth turn into cancer tumors only when their genes are heavily damaged, often through heavy use of tobacco or alcohol. This damage does not occur all at once. Prior to the growth of tumors, lesions show up in the form of red or white patches. The virus is believed to kill these pre-cancerous lesions before they metastasize into cancerous tumors.

Onyx conducted a clinical trial involving ten patients with pre-cancerous lesions in their mouths who rinsed with the flavorless solution for half an hour, once weekly for three months. Those that showed improvement were eligible for another three months of treatment. Doctors took biopsies of the tissue to see if it became more or less cancerous. Two of the ten patients saw patches completely disappear, one for nearly six months. The lesions became less severe in two others and became worse in the rest of the patients. This was a Phase II study, so it was not aimed at proving conclusively that the treatment works. While the mouthwash was not toxic, some patients did experience minor flu-like symptoms, including chills and low fevers.

In addition to the ONYX-015 program, which includes Phase I and II trials in pancreatic, ovarian, colorectal, and lung cancers, Onyx Pharmaceuticals is also developing other therapeutic viruses. These include pRB-selective viruses, which operate on the same principle as ONYX-015, and armed therapeutic viruses, which have multiple cancer-fighting capabilities.

Transgene S.A. approaches cancer therapy with its antigen-specific therapy. Recently an increasing number of antigens have been identified that are specific to cancer cells. Antigen-specific therapy is being developed to induce the body to mount a strong cellular immune response against these tumor antigens. To do this, the gene for the tumor antigen (in the case of Transgene s first product candidate, Muc1) is carried by a **vaccinia** virus, along with the gene for **IL-2** (interleukin-2). IL-2 is the main factor responsible for the proliferation of activated T cells. IL-2 also affects other components of the immune system including B cells and macrophages. The vaccinia virus vector is injected intramuscularly, where both antigen and IL2 are produced. This combination of antigen and IL2 activates **CTLs** (**cytotoxic** T lymphocyte), which can attack the cancer at all sites throughout the body. Animal studies have demonstrated that injection of Transgene s vaccinia virus vectors, carrying both tumor antigen and IL2, produces a tumor-specific CTL response with a strong anti-tumor effect.

Transgene s first product candidate for antigen-specific therapy expresses the Muc1 antigen, stimulating a cellular immune response, which may be useful in treating breast cancer, prostate cancer, and other adeno-carcinomas that produce the same antigen, such as lung, pancreatic, and ovarian cancers. Transgene completed a Phase I trial in nine women with breast cancer in which the potential product was well tolerated without serious side effects and Muc1 specific immune responses were observed.

Transgene s second product for antigen-specific therapy uses an attenuated vaccinia virus expressing two Human Papilloma Virus (HPV) antigens found in one specific sub-type, HPV 16. HPV infection is spread sexually and has been causally linked to cancer of the cervix and pre-cancerous changes in the cervix. Transgene s antigen-specific therapy product may have utility both in the treatment of metastatic cervical cancer and in preventing cervical cancer by immunizing HIV-positive women who are infected with HPV. Phase II trials are currently being initiated in North America and Europe.

Cervical cancer is diagnosed in over 130,000 women each year in the U.S. and Europe and is responsible for about 15,000 deaths annually. Over 90% of women with cervical cancer are infected with HPV, and over 60% of these are infected with HPV sub-type 16. HPV infections are particularly common and seen in the majority of women infected with human immunodeficiency virus (HIV), and the cancerous changes can progress particularly rapidly in these women.

Other Organizations and Institutions: In addition to the development efforts taking place at the aforementioned biotechnology companies, researchers at Baylor College of Medicine in Texas are placing a Herpes gene in an adenovirus and injecting it into a cancerous prostate. The virus carrying the Herpes gene easily invades the cancerous cells, making them susceptible to cancer-killing treatments with standard anti-Herpes drugs.

Doctors at Albany Medical Center Hospital in New York are also using a modified adenovirus in combination with standard chemotherapy drugs to treat ten terminally ill patients with head and neck cancers. Two patients have had complete remission and have been cancer-free for months. Among the other eight patients in the study, tumor sizes have decreased 40% to 95%.

HERPES SIMPLEX VIRUS (HSV)

Attenuated HSV mutants have proven effective in preclinical studies of breast, prostate, colon, ovarian, melanoma, neuroblastoma, and head and neck cancers. Additionally, attenuations have included tumor-selective replication and pro-drug suicide genes. The potential severity of HSV infections, however, has resulted in additional steps to ensure safety in using HSV as a cancer therapy. Cancers being treated include brain cancer and metastatic melanoma currently under development at Medigene AG and Antigenics Inc.

NEWCASTLE DISEASE VIRUS

A virus known to cause severe disease in domestic chickens, Newcastle Disease virus affects the gastrointestinal and respiratory tracts as well as the central nervous system. When the infection reaches humans, it results in a mild **conjunctivitis** and **laryngitis**. The virus has been injected into a number of patients with melanoma and colon cancer without any serious adverse events. Closely held Wellstat Biologics, formerly known as Pro-Virus, in Gaithersburg, Maryland, has demonstrated activity in a Phase I clinical trial of its compound, PV701, which is a replication-competent Newcastle Disease virus strain that is injected into the bloodstream of the patient. Using PV701 as a single agent by intravenous administration, one patient with head-and-neck cancer had complete tumor regression, two patients, one with colon cancer and the other with mesothelioma, had tumor regression of greater than 50%, and six patients with diverse malignancies (melanoma, colon carcinoma, pancreatic carcinoma) had measurable tumor reduction. Overall, 14 of 62 evaluable patients had freedom from tumor progression of between 4 and 29+ months (ongoing).

PARVOVIRUS

The parvovirus is a known cause of infections in birds and mammals, with 70% to 90% of adults seropositive (having been previously exposed to this virus). The greatest threat of this disease is in children, who are prone to developing a rash called fifth disease or slapped cheek disease. In adults, the virus causes a temporary arthritis-like joint pain. Studies of the parvovirus involve developing vectors for gene therapy for sickle-cell anemia and **thalassemias**, as well as a host of disorders such as cardiovascular disease and diabetes. The German Cancer Research Center is currently involved in preclinical studies with this virus.

POLIOVIRUS

The poliovirus enters through the stomach, infecting the intestinal lining and causing transient, self-limiting diarrhea. Approximately 1% of cases lead to neuropathogenicity involving paralysis or sometimes death. Artificial recombination of the poliovirus, along with parts of the human rhinovirus (cold virus), has demonstrated a lack of neurovirulence in primates. Additionally, the poliovirus recombinants have shown efficacy in malignant glioma cells in preclinical studies. Research within this area is being pursued at the State University of New York.

POXVIRUS

Within the poxvirus family is the highly pathogenic **smallpox** virus as well as the therapeutic virus, vaccinia. Vaccinia was the first vaccine widely used to eradicate smallpox, and also the longest therapeutically used virus in human use. While it is a relatively safe virus, it does induce a vigorous immune response that can be fatal to immunocompromised patients. This is because vaccinia s large genomic payload allows for the insertion of large fragments of **DNA**. Additionally, the virus can be modified to encode tumor-specific antigens that stimulate and direct the immune system to specifically target cancer cells or have gene-encoding, co-stimulatory molecules and immune-modulating proteins.

These enhance the immune response. In addition to being studied at Jefferson Medical College in Philadelphia, the poxvirus is also being developed at Therion Biologics, specifically for melanoma, prostate, and colorectal cancers in a recombinant form.

RETROVIRUSES

Scientists at the College of Physicians and Surgeons at Columbia University in New York City are using retroviruses in their bone marrow studies. Because retroviral therapy can only be used on cells that divide, it is very effective when used to treat tumor cells that divide rapidly. However, this treatment fails when pitted against brain and other neurological cancers, where mature cells do not replicate themselves. A family of slow-acting retroviruses, called **lentiviruses** (HIV is a lentivirus), infects both dividing and non-dividing cells. This makes lentiviruses excellent vectors to deliver gene therapy to cancers of the brain and nervous system.

VESICULAR STOMATITIS VIRUS

This virus results from direct contact with infected animals and causes flu-like symptoms such as headache, fever, retrobulbar pain on motion of eyes, malaise, nausea, and pain in the limbs and back. This virus has been shown to rapidly replicate in and selectively kill human tumor cell lines that are interferon-non-responsive. Research within this area is being developed by Wellstat Biologics, with a naturally attenuated strain of vesicular stomatitis virus called PV320. Now in its third year of development, there is evidence that it works in solid tumors and leukemia (in vitro and animal).

Evolution of Technology

Life Cycle of a Virus

A virus is an organism composed of nucleic acid in a protein coat. Viruses cannot reproduce on their own, but rather are **parasitic** and require a host in order to reproduce. Specifically, the virus must borrow the host cell s manufacturing machinery in order to replicate.

Life cycles of viruses are made up of five key steps:

(1) Absorption

(2) Entry of the nucleic acid into the cell

(3) Transcription, translation, and replication

(4) Maturation of particles

(5) Release of particles

The life cycle of a virus takes between 6 and 48 hours, though it may not always terminate with cell death. Viral infections can sometimes result in unhealthy, slow growth and potentially cell death, or in some cases, the cell will continue to release viral progency indefinitely and never die.

Logic For Using a Virus to Fight Cancer

The concept behind using a virus to fight cancer has existed for decades, dating back to the early part of the 20th Century based on the theory that the viral attack was stimulating an anti-tumor immune response rather than a direct destruction of the tumor. In 1912, there was a report where regression of cervical carcinoma was observed after inoculation of patients with an attenuated rabies vaccine. Reports were then published in the early 1920 s showing viruses replicating and lysing experimental tumors. This premise was tested in the late 1940 s in intentional inoculations of live viruses into human patients.

The 1950 s, 1960 s, and the early 1970 s gave way to more extensive research on the following oncolytic viruses in patients: adenovirus; mumps; measles; bovine enterovirus; Newcastle Disease virus; Egypt 101; HSV; West Nile; Ilheus; and Bunyamwera viruses. Specifically, the National Cancer Institute of the United States ran a 30-patient, cervical carcinoma trial of adenovirus in 1954-1955. In this trial, two-thirds of the patients displayed marked to moderate local tumor response, with liquefaction and ulceration of the injected tumor mass. The seven control patients did not respond to the virus, nor did the virus inoculations lead to any serious side effects. An early study in 1962 involving 27 healthy prison inmates inoculated with reovirus strains of all three serotypes concluded that no significant safety issues other than temporary mild symptoms existed. These inmates were observed for 23 days following inoculation. Notwithstanding results from the aforementioned early-stage research, virotherapy was not taken further at that time due to the limited clinical efficacy, unpredictability of responses, and the development of more active chemotherapeutic agents. Furthermore, there was no ability at that time to facilitate large-scale production of purified virus, nor was there the capability to quantify the biologic activity.

The doors once again opened in 1991, following a publication in *Science* magazine about a study conducted at Georgetown University using the Herpes simplex 5 virus for the treatment of brain cancer. Now a more widely known field, oncolytic viruses, or human viruses that infect and replicate in cancer cells, were being used to destroy harmful cells, all the while leaving normal cells largely unaffected. Like all viruses, oncolytic viruses look to penetrate a host cell and trick it into replicating more of the virus, ultimately bursting the cell. Unlike other viruses, however, oncolytic viruses sought only to replicate within cancer cells.

In 1998, researchers at the University of Calgary, including Matthew Coffey (now Vice President, Product Development for Oncolytics Biotech), discovered the reovirus cancer-killing qualities. They demonstrated that the reovirus preferentially killed cancer cells that possessed

abnormal RAS signaling pathways. They published their results in a paper printed in *Science* magazine, where they introduced the oncolytic effects of the reovirus. With its generic attachment strategy, the reovirus demonstrated the potential to target most cells since it was dependent on an activated RAS **proto-oncogene** pathway for protein translation, thus enabling productive infection and host cell death only in a subset of cells. The researchers realized the potential for this technology and made a decision to patent the technology. The following year, they turned it over to a new company, Calgary-based Oncolytics Biotech, with the idea that the Company could turn it into a legitimate cancer treatment.

Virotherapy Gains Increasing Attention

Oncolytic viruses are believed to have a significantly higher therapeutic index than existing chemotherapies, meaning that oncolytic viruses are more specific in targeting and killing tumor cells while leaving healthy cells untouched. The Company believes, based on the preclinical and Phase I evidence, that the therapeutic index of the reovirus is at least 1,000:1. In fact, the Company has not seen any dose-limiting toxicity in any animal or human study conducted to date.

RAS and Its Link to Cancer

The RAS protein plays a pivotal role in the growth pathway in numerous cell types. Over-activation of RAS is implicated in numerous cancers. Thus, inhibition of RAS has attracted significant interest for its therapeutic potential. The RAS pathway is one of several complex and cross-linked pathways that transfer growth signals from the surface of the cell to the nucleus. In normal cells, the process is controlled and appropriate signaling takes place. In a significant percentage of cancer cells, a mutation has occurred along this pathway that prevents the cell from switching off the signal, encouraging uncontrolled cell growth. Figure 4 (page 21) illustrates the process of how the reovirus is activated in a cancer cell vis-à-vis an activated RAS pathway.

Scientists have identified a range of 30% to 90% of human cancers with mutations along the RAS pathway. Activating mutations in the RAS protein itself is estimated to occur in approximately 30% of all human tumors and since RAS and the RAS pathway play a central role in signal transduction, the RAS pathway is a potential target for approximately two-thirds of all cancers including pancreatic, sporadic colorectal, lung carcinomas, and myeloid leukemia.

Oncolytics Biotech s Technology REOLYSIN®

REOLYSIN® is Oncolytics Biotech s trademark name for its reovirus technology, which infects, multiplies, and destroys mammalian cells with an activated RAS pathway. The technology has demonstrated extremely high potency in a number of cancer models. Specifically, the broad applicability of the reovirus therapy to many different cancers was demonstrated in several separate tissue culture assessments. Compared to some of the other oncolytic viruses under development, reovirus tumor killing does not appear to be due to a host immune system attack on the implanted cancer. Simultaneously, the Company believes that the potential effectiveness of the reovirus is not expected to be compromised by a functional immune system, although dosage and delivery may be impacted.

Since activation of the immune system is not the mechanism by which the reovirus kills cancer cells, when the reovirus is administered to a patient population with either a variable or a depressed immune system, it should turn out to be uniformly efficacious in patients with differing levels of immune competency. Consequently, the Company maintains that reovirus therapy should permit the destruction of cancerous cells while neighboring cells remain unaffected.

The Company has stated that it has targeted REOLYSIN® initially as a local tumor treatment in an effort to expedite clinical trial completion and next plans to target systemic metastatic therapy, since metastatic cancer is the major concern in the modern cancer arena, responsible for the most cancer-related deaths. We provide a snapshot of the potential indications that Oncolytics Biotech may seek in developing REOLYSIN® in Table 3.

Preclinical Studies

REOLYSIN® has been extensively tested in mouse models of cancer, including various lymphomas, breast, ovarian, colon, glioma, and pancreatic cancers. The reovirus has been successfully administered by several routes including direct injection into solid tumors, systemic administration, inhalation into the lungs, and injection into the brain. Low levels of reovirus-specific antibodies do not affect systemic activity and short treatments with approved immune suppressant drugs successfully reduce the antiviral effect of high antibody levels.

Oncolytics has reported results from two studies examining the use of REOLYSIN® in companion pet dogs with naturally occurring cancers. The safety of REOLYSIN® was examined in dogs and there were no serious adverse reactions related to the treatment. Efficacy was assessed by both measurement of tumor response and by **histopathological** (i.e. looking at changes at the cellular level) comparison of pre-treatment and post-treatment tumor biopsies. The level of activity was very similar to that observed in the first human clinical trial.

The Company has an ongoing **GLP** (good laboratory practices) toxicology program, in which nine studies have examined three different routes of delivery in three animal species. The results to date have shown no serious adverse events and no dose-limiting toxicity in animals.

Phase I Clinical Trial

Oncolytics Biotech announced summary results in March 2002 from its Phase I clinical trial of REOLYSIN® that was initiated in June 2000 through the Tom Baker Cancer Center in Calgary, Alberta. The study examined the administration of escalating dosages of REOLYSIN® directly into a subcutaneous (underneath the skin) tumor in 18 terminal cancer patients with progressive (actively growing) cancer that had failed to respond to conventional therapies such as surgery, chemotherapy, or radiation. These patients were terminal, with not much hope for long-term survival (up to three months life expectancy). The primary cancers included head and neck, breast, melanoma, non-AIDS Kaposi s sarcoma, and others. The injected tumors included some lesions that had metastasized. The primary endpoint of the trial was safety.

Data showed that none of the patients experienced any serious adverse events due to the virus, nor were there any dose-limiting toxicities observed in this patient group. The secondary outcomes related to tumor responses measured at both the treated lesion as well as remote tumor sites. Viral activity was defined as a transitory or lasting tumor regression of at least 30%, measured in two dimensions against the tumor size prior to injection on the first day of treatment. Evidence of viral activity was detected in 11 of 18 patients (61%), with the tumor regression ranging from 32% to 100%.

Clinically, tumor response was classified in one of four ways:

(1) progressive disease: tumor growth of greater than 25%

(2) stable disease: change ranges from growth of less than 25% to a reduction of less than 50%

(3) partial response: a reduction of greater than 50% but still detectable tumor

(4) complete response: no tumor detected

Following 28 days, only 17 of the original patients were evaluable and 11 of these showed stable disease, including two complete transient responses, despite the fact that some only received a single injection. By day 98, 5 of 10 evaluable patients still had tumor responses (4 stable disease, one partial response). It is worthy to note that there was evidence of remote tumor responses (evidence of viral activity) and tumor shrinkage in other tumors not injected. This gives early evidence of the potential of REOLYSIN® to transport to other tumors and effectively destroy them. While this efficacy evidence was not statistically significant, it further justified continuing development of REOLYSIN® and the initiation of additional clinical trials.

T2 Prostate Cancer Clinical Trial

Prostate cancer, one of the most common cancers among men, has a higher likelihood of occurrence in men as they age. The American Cancer Society estimates that the total number of new prostate cancer cases in the U.S. will reach 189,000 in 2002, with approximately 30,200 deaths (see Table 1, page 10).

Despite the stabilization of mortality rates, standard treatments have been limited to radiation therapy, radical prostatectomy (surgical removal of the prostate), and/or chemical castration. These treatments have been successful at stabilizing mortality, but they have increased rates of morbidity. Specifically, these treatments have reduced the quality of life through anal injury, urinary incontinence, urethral stricture, and impotency. The need is clear that this disease needs less toxic and austere measures of treatment. Oncolytics Biotech believes that the level of RAS activation in prostate cancer is approximately 60%, based on the levels of mutation and over-expression of RAS pathway components found by other researchers.

In May 2001, Oncolytics Biotech filed a Canadian Investigational New Drug (IND) application for the first Phase II clinical trial for REOLYSIN®, examining the efficacy of intra-tumoral injection for the treatment of Stage T2 (T2a and T2b) prostate cancer. T2 prostate cancer is defined as a tumor that is confined to the prostate and is detectable during a digital rectal exam as a hard lump on the prostate. If it is confined to one side of the gland (right or left) and if less than two centimeters in diameter, it is considered a T2a prostate cancer. If it involves both sides of the prostate gland or is larger than two centimeters, it is considered a T2b prostate cancer.

According to the Company, the trial will enroll up to 45 patients at two clinical sites who will be injected in the prostate lesion with a single dose. Three weeks after injection, a prostatectomy is performed as part of the standard treatment for prostate cancer, at which point the prostate is examined for viral activity and tumor response. Primary endpoints are to determine the safety and histologic efficacy. Histologic efficacy is to assess the treated and excised prostate for evidence of tumor regression. Secondary endpoints include assessment of patient antibody development and patient toxicity. The Company believes that the trial enrollment could be complete by the second quarter of 2003, a year after initiated.

Phase I/II (Malignant Glioma/Glioblastoma)

Over the past 30 to 40 years, improvements in conventional treatments for brain cancer have essentially failed to extend patients lives for very long. There has been surgery, chemotherapy, and radiation all treatments that remain comparatively ineffective for brain cancer versus a disease such as leukemia, which is typically responsive to such treatments. Brain cancer, or malignant glioma, which in its most common and aggressive form is known as glioblastoma, is extremely poorly responsive to treatment.

It carries a median survival time of about 11-14 months from first occurrence and represents approximately 35% of the estimated 17,000 malignant brain tumors, or 6,000 new cases in the U.S. annually (See Table 1, page 10).

Glioblastoma can be found anywhere in the brain or spinal cord and is more commonly found in older adults, especially men. The first sign is usually increased pressure in the brain from a rapid tumor growth, causing headaches, seizures, memory loss, and a change in behavior. The principle reason that this type of cancer is so difficult to treat is the need to avoid removing or destroying normal brain tissue, which may result in severe side effects including the patient s ability to move or speak. In preclinical testing, 20 of 24 glioma cell lines and 9 out of 9 glioma biopsies were susceptible to the reovirus.

Typically, glioblastoma is treated by surgery to remove as much of the tumor as possible. It is then followed by radiation and/or chemotherapy (noting that chemotherapy is also used before and during surgery). A common drug treatment for this type of cancer is the GLIADEL® Wafer by Baltimore-based Guilford Pharmaceuticals. This treatment has shown to increase survival, with a multinational Phase III clinical trial to assess the survival benefit for newly diagnosed patients given GLIADEL® Wafer showing that the median survival increased from 11.6 months for patients given placebo wafer to 13.9 months in patients given GLIADEL® Wafer. At one year, 59% of patients given GLIADEL® Wafer were still alive compared to 48% of those given placebo.

Oncolytics Biotech filed a clinical trial application in January 2002 with Health Canada to initiate a Phase I/II clinical trial using REOLYSIN® to treat malignant glioma. The Company also filed an IND with the U.S. FDA in March 2002. The study is presently being conducted in Calgary at the Tom Baker Cancer Centre, with plans to expand to other centers in the U.S. and Canada.

The Phase I portion of the study is a dose escalation study in 12-24 patients with a variety of recurrent gliomas. The Phase II portion will treat patients at the dose selected from the dose escalation study with up to 14 recurrent glioblastoma multiforme patients. Assuming results are positive, the Company expects to advance this indication into Phase III clinical trials. Similar to GLIADEL®, which improved survival time by two months, trials such as these have the potential to run quickly, with the possibility for fast-track designation. If this occurs, an expedited FDA review could take place, as well as a faster acceptance among the medical community given the limited alternatives.

Oncolytics Biotech announced in late December 2002 positive interim safety results from the Phase I component of its clinical study examining the use of REOLYSIN® in the treatment of recurrent malignant glioma. The Company reported that REOLYSIN® appeared to be well tolerated when surgically delivered into the brain during the treatment of the first six patients. Determination of the safety of REOLYSIN® is the primary purpose of the Phase I study. The study is to examine the use of a single, intratumoral injection of REOLYSIN® delivered using imaging-guided surgery, in patients with malignant glioma that has recurred despite other treatments, including surgery and radiation therapy. After treatment with REOLYSIN®, the Phase I patients are monitored and evaluated for safety for a period of six months.

Systemic Administration

Oncolytics Biotech presently intends to initiate a Phase I/II study in 2003 to deliver REOLYSIN® through a systemic means to treat inoperable forms of liver, non-small cell lung, or pancreatic cancer. This type of delivery would involve intravenous drug delivery, although other future forms of delivery may include oral liquid. Preclinical studies have shown REOLYSIN® s ability to travel throughout the body systemically and cause regression of tumors that are remote from the point of entry. A clinical trial for such an indication would initially be performed as a Phase I dose escalation study. Once the maximum tested dose is reached, the Phase II trial would begin with a larger group of patients using a single protocol.

Risks

Some of the risks associated with investing in Oncolytics Biotech are similar to those of other development-stage biotechnology companies. These are referenced below in the Competition , Product Risks , and Other Risks sections. Additionally, except for the historical information contained herein, the matters discussed in this Executive Informational Overview are forward-looking statements that involve risks and uncertainties that could cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include the Company s ability to raise additional capital, conduct successful clinical trials, obtain regulatory approvals, and gain acceptance from the marketplace for its products.

Additional risks are set forth in the Company s Annual Report on Form 20-F for the year ended December 31, 2001 filed with the Securities and Exchange Commission on April 1, 2002, and the Company s Quarterly Reports on Form 6-K for the quarters ended March 31, 2002, June 30, 2002, and September 30, 2002. The Company undertakes no obligation to publicly release the result of any revisions to these forward-looking statements that may be made to reflect events or circumstances after the date hereof, or to reflect the occurrence of unanticipated events.

Competition

A host of pharmaceutical, biotechnology, and other organizations are currently developing anti-cancer drugs, including five multi-national pharmaceutical giants Merck & Company, Schering Plough Corporation, Johnson & Johnson, Bristol-Myers Squibb Company, and Bayer. Additionally, there are over one half-dozen companies targeting the area of virotherapies with recombinant viruses, such as HSV, poliovirus, and adenovirus. Other companies that are targeting the RAS pathway as a means to block cancerous growths, include Bristol-Myers Squibb Company, Isis Pharmaceuticals, and Johnson & Johnson. Each of these companies has greater financial means than Oncolytics Biotech and thus more resources at hand for developing their compounds.

Product Risks

With regard to REOLYSIN®, while the therapy has shown success in animal models, tissue culture, human tissue specimens, and a Phase I human trial, there is no guarantee that similar success will be seen in future trials in humans. The reovirus has not proven to be pathogenic in humans in any published scientific or medical study in over 40 years since it was discovered, despite the fact that 70% to 100% of humans have been exposed to the virus. The reovirus has been shown to be safe and well-tolerated in nine GLP toxicology studies conducted for Oncolytics Biotech and in all human clinical trials to date. The virus has also shown exceptional genetic stability since its discovery.

During the course of the development for REOLYSIN®, Oncolytics Biotech will continue to assess the safety of the product. However, the reovirus did cause some morbidity in SCID mice, the equivalent of humans that have essentially no immune system. Therefore, there is a potential risk that the product could cause severe side effects in some patient populations, who would not be eligible for treatment, or that a previously unobserved side effect or mutation could occur.

Other Risks

Oncolytics Biotech is an early-stage biotechnology company whose long-term success depends largely on the successful development and marketing of its lead and presently its only drug candidate, REOLYSIN®. There is no guarantee that any drug in human clinical trials will be successfully approved for therapeutic use. Additionally, early-stage biotechnology companies require substantial amounts of capital during their development process. To date, the company has been successful in raising needed capital to fund its business. There is no guarantee that it will be able to raise such funds in the future. Also, as with other smaller emerging stage companies, the Company is dependent on several key employees, making them vulnerable should they lose any part of their management team.

Recent Highlights

Oncolytics Biotech recently received approval from Health Canada and subsequently commenced a Phase I/II clinical trial for recurrent glioblastoma (brain cancer).

Oncolytics Biotech commenced and continues enrollment in a clinical trial for T2 prostate cancer.

Oncolytics Biotech acquired minority interest in two Canadian biotechnology firms Transition Therapeutics Inc. and BCY LifeSciences, Inc. potential investments that could expand its product pipeline.

Oncolytics Biotech received favorable safety and efficacy results in a third party research program examining the use of REOLYSIN® for the treatment of cancer in dogs.

Oncolytics Biotech strengthened its management through the addition of Dr. George Gill, Vice President of Clinical Regulatory Affairs (see Management section, page 6).

Oncolytics Biotech strengthened its Board of Directors through the additions of both Mr. George Masters and Dr. William A. Cochrane(see Board Member section, page 7).

Oncolytics Biotech recently received its fifth U.S. patent covering REOLYSIN(R)technology.

Points to Consider

Clinical data suggest that oncolytic viruses may offer therapeutic advantages over existing cancer therapies such as chemotherapy and radiation. The primary benefits identified to date are listed below and are the basis of Oncolytics Biotech s key investment considerations:

Compared to other types of cancer therapeutics, oncolytic viruses including REOLYSIN®, have not caused significant side effects. Traditional chemotherapy treatments can lead to hair loss, nausea, and anemia. Radiation is highly toxic to the body.

High therapeutic index. Oncolytics viruses are believed to have a significantly higher therapeutic index than existing chemotherapies, meaning that oncolytic viruses are more specific in targeting and killing tumor cells while leaving healthy cells untouched. The Company believes, based on the preclinical and Phase I evidence, that the therapeutic index of the reovirus is at least 1,000:1.

Phase I human study. The Company announced final results on March 21, 2002 of its initial Phase I human study. No patients in this study experienced any serious adverse events related to the virus at any dosage. Evidence of viral activity in tumors was observed and evidence of remote tumor response was also noted.

*T2 prostate cancer study.*The Company plans to enroll up to 45 patients who have confirmed, T2 stage prostate cancer.

Phase I/II recurrent brain cancer study. The Company has commenced enrollment in a clinical trial in up to 38 patients who have recurrent malignant gliomas, one of the most aggressive and deadly forms of brain cancer.

Systemic study. The Company has stated that it expects to begin a study in 2003 to examine the effects of the systemic administration of REOLYSIN® on a yet-to-be-determined form of cancer.

Patent protection. The Company has strong patent protection, with 5 U.S. patents issued and approximately 100 applications for protection in 15 patent families.

Partnerships. The Company is in continued discussions with strong interest from several potential partners.

Product pipeline. The Company has recently acquired minority interests in two other Canadian biotechnology companies--Transition Therapeutics Inc. and BCY LifeSciences Inc.--potentially giving it access to other technologies for possible future expansion.

CONCLUSION:
Assuming that Oncolytics Biotech aligns with a partner and REOLYSIN®successfully completes testing and is approved, the Company believes that REOLYSIN® could reach the market within the next three to four years.

Glossary of Lesser-Known Terms

Adenovirus: Infection which leads to cold-like symptoms.

Androgen: Male sex hormone that promotes the development and maintenance of male sex characteristics. The major androgen is testosterone.

Angiogenesis: Process of developing new blood vessels; important in the normal development of the embryo and fetus. Also appears important to tumor formation.

Antiangiogenesis: Process in which the tumor s blood supply is inhibited by blocking the formation of new blood vessels.

Antibody: Y-shaped protein on the surface of B cells that is secreted into the blood or lymph in response to the presence of an antigen.

Antigen: Protein on the surface of a cell capable of inducing a specific immune response.

Apoptosis: Process leading to controlled cellular self-destruction (cell suicide).

Cancer: Family of diseases in which cells grow and spread uncontrollably throughout the body disrupting the balance between new cell growth and old cell death.

Conjunctivitis: Inflammation of the conjuctivae, the membranes on the inner part of the eyelids and the membranes covering the whites of the eyes. These membranes react to a wide range of bacteria, viruses, allergy-provoking agents, irritants and toxic agents. Viral and bacterial forms of conjunctivitis are common in childhood. Conjunctivitis is also called pinkeye and red eye.

CTL: Cytotoxic T Lymphocyte.

Cytotoxic: Capable of killing cells.

DNA (deoxyribonucleic acid): Building block of living organisms, found primarily in the nucleus of a cell, that carries the genetic information in a cell and is able to self replicate and synthesize RNA.

Enteric: Of or relating to the small intestine.

Enzyme: Protein (or protein-based molecule) that speeds up a chemical reaction in a living organism. An enzyme acts as catalyst for specific chemical reactions, converting to a specific set of reactants (called substrates) into specific products.

Gene: Hereditary unit (comprised of DNA) that carries the instructions for making the thousands of proteins needed for a specific cellular function. Certain diseases are associated with the absence or malfunction of a specific gene.

Glioma: Brain cancer.

GLP: Good laboratory practices.

Histopathological: Looking at changes at a cellular level.

hTERT: Human Telomerase Reverse Transcriptase, the catalytic protein component of human telomerase.

IL-2 (Interleukin-2): Main factor responsible for the proliferation of activated T cells. IL-2 also effects other components of the immune system including B cells and macrophages.

In vitro: A process that takes place under artificial conditions or outside of the living organism.

In vivo: Inside the living body.

Intratumoral: Into a tumor.

Intravenous: Into a blood vessel.

Laryngitis: Inflammation of the larynx.

Lentiviral Vector: Viral gene delivery system engineered for *in vivo* delivery of therapeutic genes into both dividing and non-dividing cells. Lentiviruses have the capability to insert a significant amount of genetic information directly into the DNA blueprint of the host s cells making the lentivirus one of the most efficient methods of gene delivery.

Lysis: Destruction.

Metastasis: Process by which cancer spreads from a primary location in the body to other healthy tissues located elsewhere in the body via the lymphatic and circulatory systems.

Micrometastasis: Spread of undetectable cancer cells.

Monoclonal antibodies: Synthetic antibodies. Chemicals or radiation tagged to the MAB may be delivered directly to tumor cells. Or, the MAB itself may be capable of tumor cell destruction.

Oncogene: Fragments of genetic material (DNA) that carry the potential to cause cancer (transform normal cells into malignant cells).

Oncology: Branch of medicine that deals with tumors, including study of their development, diagnosis, treatment, and prevention.

Oncolytic virus: A virus that selectively replicates in and kills cancer cells. Oncolytic viruses like the reovirus have been found to be significantly more specific for killing cancer cells than standard chemotherapeutic drugs.

P53 tumor suppressor protein: Involved in multiple central cellular processes, including transcription, DNA repair, genomic stability, senescence, cell cycle control, and apoptosis. p53 is functionally inactivated by structural mutations, interaction with viral products, and endogenous cellular mechanisms in the majority of human cancers. This functional inactivation can, in some circumstances, produce resistance to DNA-damaging agents commonly used in cancer chemotherapy and radiotherapeutic approaches.

Parasitic: Having to do with a parasite, as in a parasitic infection; or acting like a parasite by taking nourishment from another.

Pathogenic: Causing disease, or capable of doing it.

PKR: Protein kinase R. Responsible for the cellular "antiviral" response to reovirus in normal cells. Not effective when RAS pathway mutation occurs.

Prostate-specific antigen (PSA): Chemical substance produced only in the prostate. A prostate-specific antigen level above normal may indicate prostate enlargement or cancer, and signals prompt further investigation.

Protein: Complex molecules responsible for specific and unique functions within the body. Examples of proteins include hormones, enzymes, and antibodies.

Proto-oncogenes: Fragments of genetic material (DNA), related to oncogenes, but are the normal "switches" used to control growth and tissue repair.

RAS gene: Gene acts as a controller a dispatcher that passes on biochemical signals to cells. The signals, in the form of proteins, tell the cell when to divide and when to stop dividing.

RAS pathway: Signal transduction cascade, or series of proteins linked from the surface of the cell to the RAS protein transmitting growth signals.

Reovirus: Naturally occurring virus believed to cause mild, sub-clinical infections of the upper respiratory and gastrointestinal tract of humans, though may be used to eliminate cancer tumors.

RNA (ribonucleic acid): Single-stranded nucleic acid, the primary function of RNA in a cell is the step between DNA and protein synthesis. RNA is a component of telomerase and is responsible for acting as a template on which the telomere repeats are made.

Smallpox: Highly contagious and frequently fatal viral disease characterized by a biphasic fever and a distinctive skin rash that left pock marks in its wake. Because of its high case-fatality rates and transmissibility, smallpox now represents a serious bioterrorist threat.

Somatic cell: Any cell in the body other than an egg or sperm.

Systemic: Circulating throughout the body.

Telomerase: Enzyme composed of a catalytic protein component and an RNA template, which synthesizes DNA at the ends of chromosomes and confers replicative immortality to cells.

Thalassemias: Blood disorder that is not one disease but rather a group of disorders that have a single feature in common: they all have a genetic defect in the production of hemoglobin, the protein that enables red blood cells to carry oxygen.

Therapeutic Index: Ratio of the effective drug dose versus the dose that causes toxicity.

Vaccine: Treatment intended to mimic and thereby prevent a natural infection, without the risks of a natural infection.

Vaccinia: Live virus within the vaccine that is used to prevent smallpox.

Vector: Vehicle by which genes are transported into cells thereby allowing cellular genetic modification to occur. Viral vectors are viruses rendered incapable of reproducing themselves and non-viral vectors include naked DNA or lipid coated DNA.

Virotherapy: Unique cancer therapy that seeks to harness the natural properties of viruses, whether altered, attenuated or naturally occurring, to aid in the fight against cancer while at the same time maintaining healthy normal cell function.

Virus: Microorganism that requires a host organism in order to grow and replicate. A replicating virus integrates its genetic information (DNA or RNA) into the host cell overriding the host cell s biological mechanism in order to reproduce new virus particles.

Wild-type: Naturally occurring, or non-engineered.

Note Regarding Forward Looking Statements

Certain statements in this document constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are statements that are not historical facts, and include but are not limited to: the Company s financial projections and estimates and their underlying assumptions; statements regarding plans, objectives and expectations with respect to product research and development, clinical testing and commercial applications of the Company s technologies; the impact of regulatory requirements on the Company s products; the potential markets and applications for the Company s products; assumptions related to the pharmaceutical industry and the Company s competitors; and statements regarding future performance. Forward-looking statements generally, but not always, are identified by the words expects, anticipates, believes, intends, estimates, projects , potential , possible and similar expressions, or tha conditions will, may, could or should occur. Such forward-looking statements involve known and unknown risks, uncertainties and other factor which may cause the actual results, performance or achievements of Oncolytics Biotech Inc. (the Company), or industry results, to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Such risks and uncertainties include, among others, the following:

- the Company s primary potential product, REOLYSIN®, is in the research and development stage and is unlikely to be commercially available for a number of years, if at all;
- the Company s success depends on its patents and its ability to protect its intellectual property rights;

the Company has a history of operating losses and future profitability is uncertain;

the Company anticipates that it will require additional capital to complete research, development, and testing of its products and the availability of such capital on acceptable terms is uncertain;

the Company has limited manufacturing or marketing experience and will likely depend on strategic partners to commercialize its products;

the Company's success depends on the skills of its management and employees;

REOLYSIN® is in various stages of clinical trials for T2 prostate cancer and malignant glioma, and these clinical trials are long and expensive processes which will likely determine the commercial feasibility of REOLYSIN®;

the Company must obtain approval for its products from and meet the requirements of the Food and Drug Administration in the United States or the Health Protection Branch in Canada to commercially market its products;

the biotechnology industry is extremely competitive and the Company competes against companies with significantly greater financial and other resources;

the Company's products could fail or cause harm to patients which could subject the Company to product liability claims; and

other possible risks that are further described in the section entitled Risk Factors contained in the Company s annual report on Form 20-F for the year ended December 31, 2001, and the Company s quarterly reports on Form 6-K for the quarters ended March 31, 2002, June 30, 2002 and September 30, 2002, each filed with the United States Securities and Exchange Commission.

Such forward-looking statements are made as of the date of this report and management assumes no obligation to update such forward-looking statements. You are cautioned against placing undue reliance on forward-looking statements.

Other Notes & Disclosures

The content of this report with respect to Oncolytics Biotech has been compiled primarily from information available to the public released by Oncolytics Biotech through news releases and SEC filings. Information as to other companies has been prepared from publicly available information and has not been independently verified by Oncolytics Biotech. Certain summaries of scientific activities and outcomes have been condensed to aid the reader in gaining a general understanding. For more complete information about Oncolytics Biotech, the reader is directed to the Company s website at www.oncolyticsbiotech.com. For more detailed information on the companies listed in the competitive review, please refer to their publicly available information, including their regulatory or SEC filings. This report is published solely for information purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance.

Free additional information about Oncolytics Biotech and its public filings, as well as free copies of this report can be obtained in either a paper or electronic format by calling 212.825.3210.

To schedule an appointment with management or for further information investors should contact:
Gino De Jesus, Jeffrey J. Kraws, or Dian Griesel, Ph.D.

The Investor Relations Group, Inc.
50 Pine Street 6th floor
New York, NY 10005

T: 212-825-3210
F: 212-825-3229