








HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

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Hepatitis C Victims Fight for Secret Files -Haemophiliacs in Court Move Demand to See Official Papers

*Liam McDougall, Health Correspondent
Source: Sunday Herald*

HAEMOPHILIACS who contracted deadly liver diseases from NHS blood products have demanded the release of 600 classified documents which they believe show the government is liable for their illnesses.

Campaigners infected with hepatitis C have written to the Scottish and Westminster health ministers, Malcolm Chisholm and John Reid, calling on them to open files containing information on blood policy decisions taken by the UK government between 1972 and 1986, during which time thousands became ill.

The documents have been kept secret since 1990, when the government refused to reveal their contents to patients who were suing after contracting HIV through the NHS. According to court papers, judges who saw the documents believed the government had a case to answer but, at a time when hundreds were dying from Aids, recommended that those infected accept the government's offer of compensation rather than fight a lengthy court battle.

Since then, the documents – which relate largely to matters of policy – have been kept secret and given “public interest immunity”.

Now, the Manor House Group, formed by haemophiliacs infected with hepatitis C, say the papers could reveal how thousands of patients contracted the disease after having blood transfusions and clotting treatments. They want a public inquiry into how more than 5000 people were infected through blood products from the 1970s to the 1990s. More than 1000 have died.

Peter Mossman, the group's vice chairman, has written to John Reid demanding the files are made public. He stated: "Successive health ministers have always said if any other information was forthcoming, they would look into it. The Manor House Group believes not all the relevant information is in the public domain."

Last week, individual haemophiliacs also wrote to Reid and Chisholm calling to have the files released under incoming freedom of information legislation.

Bruce Norval, of Fortrose, near Inverness, wrote to Chisholm, citing new freedom of information rules. He said: "These documents are of direct relevance to my case as a haemophiliac infected with viruses through contaminated blood products given to me by the NHS. The scale of the disaster inflicted on Scotland's haemophiliacs was avoidable."

Mike Kenwright, a haemophiliac from Cheshire who contracted hepatitis C, said: "These 600 documents lie hidden in the Department of Health. I would ask whether they have been hidden because of what they would prove. I believe these documents will show the government was negligent in allowing thousands of us to become infected."

According to court papers seen by the Sunday Herald, the 600 documents contain a number of sensitive pieces of information, including details of exchanges between ministers and senior officials on how policy decisions were arrived at.

Campaigners believe the dates which the documents relate to are significant because at that time the UK pool of donors of the Factor VIII clotting agent expanded from around 200 to about 15,000, increasing the level of risk to haemophiliacs.

Norval added: "The government has said it believes all information is in the public domain but that it would consider any new evidence. Well, here is new evidence."

Opposition politicians also called on the government to release the information.

The fresh calls to reveal the documents come days after details of a government ex-gratia payment scheme were announced. The Skipton Fund, which will give infected haemophiliacs up to £45,000 each, is due to take claims from next month. However, several haemophiliacs called the fund only to be told that the application forms were not yet ready.

Asked about Norval's letter, an Executive spokeswoman said: "The health minister's office has just received the letter. We will consider it and respond in due course."

A Department of Health spokesman said he could not comment on any letters as they had not yet been received.

He added: "The government does not accept that any wrongful practices were employed and does not consider a public inquiry justified, as it does not believe any new light would be shed on this issue as a result."

June 7th, 2004

Sirna Therapeutics Demonstrates Systemic Efficacy of siRNAs in Multiple Animal Models

Source: PRNewswire

BOULDER, Colo.-- Sirna Therapeutics, Inc. (NASDAQ:RNAI) today announced in a presentation at the BIO 2004 Annual International Convention that it has demonstrated reproducible and robust preclinical systemic efficacy using its proprietary chemically modified and formulated short interfering RNAs (siRNAs). Nassim Usman, Ph.D., Sirna's Senior Vice President and Chief Operating Officer, presented the Company's preclinical results during today's morning panel discussion, "RNAi: The New Frontier in Gene Silencing."

Dr. Usman reported, "About a year and a half ago, Science Magazine named RNAi, or RNA interference, as the leading scientific 'Breakthrough of the Year.' Sirna has overcome major hurdles to transform this breakthrough science into a clinical-stage compound and to establish a robust portfolio of preclinical leads. The Company and its collaborators have demonstrated systemic efficacy in several different animal models of disease, using routes of administration that are appropriate for a human therapeutic."

Using normal systemic delivery Sirna researchers have achieved a reproducible one-log reduction of hepatitis B (HBV) viral DNA and S-antigen in a preclinical animal model using Sirna's proprietary modified siRNAs. The Company is using HBV as a surrogate model of hepatitis C (HCV) infection. Based on these groundbreaking results the Company expects to select an HCV clinical candidate by the end of this year.

As a further demonstration of the remarkable power of the RNAi mechanism and Sirna's proprietary modified siRNAs, the Company has developed siRNAs that provide long-term duration of effect in an animal model. Sirna researchers, in collaboration with Dr. Beverly Davidson, Professor at the University of Iowa, have achieved a 75 - 95% knockdown of a target gene (Green Fluorescent Protein) in the livers of transgenic animals for periods up to 3 weeks following a single, normal intravenous injection.

In addition to the Company's work on systemic efficacy, Sirna has successfully demonstrated efficacy in three different animal models of ocular angiogenesis including choroidal neovascularization (CNV) using two different routes of local administration. Following a pre-IND meeting with the FDA in March of this year, the Company is on schedule to file its IND in the fourth quarter of this year for Sirna-027, a chemically modified siRNA targeting VEGF Receptor-1. The Company is completing toxicology and manufacturing of clinical trial material for Sirna-027, and is finalizing the Phase I clinical protocol in collaboration with three investigators.

Sirna Therapeutics further announced that Howard Robin, Sirna's President and Chief Executive Officer, will present information on the Company's progress in a corporate presentation on Tuesday, June 8th at 10:45 AM Pacific Time during the BIO 2004 conference.

About Sirna Therapeutics

Sirna Therapeutics is using its proprietary technology and expertise in nucleic acids to develop a new class of nucleic acid-based therapeutics involving RNA interference. RNAi is a mechanism used by cells to regulate the expression of genes and replication of viruses. The RNA interference mechanism uses short interfering RNA (siRNA) to induce the destruction of target RNA using naturally occurring cellular protein machinery. Harnessing the natural phenomenon of RNAi holds potential for the development of a new class of drugs with specificity towards a wide range of diseases that result from undesirable protein production or viral replication. More information on Sirna Therapeutics is available on the company's web site at www.sirna.com.

Statements in this press release which are not strictly historical are "forward-looking" statements which should be considered as subject to many risks and uncertainties, including early stage of development and short operating history, ability to achieve and maintain profitability, ability to obtain and protect patents, risk of third-party patent infringement claims, ability to engage collaborators, ability to obtain regulatory approval for products, concentration of stock ownership, and availability of materials for product manufacturing. These and additional risk factors are identified in the Company's Securities and Exchange Commission filings, including the Forms 10-K and 10-Q and in other SEC filings. Sirna undertakes no obligation to revise or update any forward-looking statements in order to reflect events or circumstances that may arise after the date of this release.

For further information, please contact Howard W. Robin, President & CEO of Sirna Therapeutics, Inc., +1-303-449-6500; or Investors, E. Blair Schoeb, or Media, Justin Jackson, both of Burns McClellan, Inc., +1-212-213-0006, for Sirna Therapeutics, Inc.

Source: Sirna Therapeutics, Inc.

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Genetic Vaccine Promising Against Chronic Hepatitis C

Source: Karolinska Institutet

A potential vaccine candidate against chronic hepatitis C (HCV) infections is presented in a thesis from Karolinska Institutet. The new genetic vaccine can activate immune responses that are needed to clear HCV, a disease that today is difficult to treat effectively.

The hepatitis C virus (HCV) is a major cause of chronic liver disease worldwide. It is estimated that HCV affects approximately 170 million people around the world. Today, no vaccine is available to prevent or cure HCV infections. Antiviral therapy is used quite effectively, but in 60-80 per cent of the patients become chronic carriers of the virus in their liver. One feature of HCV infection is the high rate of viral persistence. The mechanism of viral persistence is largely unknown, although the high genetic variability is thought to play a key role.

In Lars Frelin's thesis the HCV NS3 protein is studied in detail since it performs key functions in the viral life cycle. These are unwinding and strand separation of the viral RNA and proteolytic processing of the precursor polyprotein. To obtain the complete protease the NS4A co-factor was included in the NS3-based vaccines. NS4A has been shown to enhance the stability of NS3 and to target the NS3/4A complex to intracellular membranes. The latter is most likely of importance for the formation of the replication complex. Also, the NS3 region has a limited genetic variability and several studies have now demonstrated that NS3-specific CD4⁺ and CD8⁺ T-cell responses are crucial for the resolution of HCV infections. Thus, several factors suggest that the NS3 region should be well suited for vaccine development.

The results show that HCV NS3-based genetic vaccines effectively primed both humoral and cellular immune responses in mice. NS3/4A was shown to prime a Th1 CD4⁺ T-cell response. The inclusion of NS4A in NS3-based vaccines primed antibody, CD4⁺, and CD8⁺ T-cell responses that were superior to those primed by NS3-gene alone. Thus, NS4A enhanced the immunogenicity of NS3. The studies also show that enhancement of the immunogenicity was most probably a result of the higher expression levels of NS3 generated by the inclusion of NS4A. Further results show that the overall immunogenicity of NS3/4A could be further enhanced by codon optimization or by mRNA amplification using the Semliki forest virus (SFV) replicon. The NS3 protein expression levels were further improved by either codon optimization and mRNA amplification. Subsequently, both these modifications enhanced the NS3-specific immune responses. One concern in development of genetic vaccines is that the gene displays unwanted properties when expressed in vivo. Therefore, a new transgenic mouse expressing the HCV NS3/4A protein in the liver was generated. The protein expression was restricted to the liver to mimic the in vivo situation during a HCV infection. Protein expression was localized to the cytoplasm of the hepatocytes and displayed a similar staining pattern as seen in hepatocytes from HCV infected individuals. The intrahepatic protein expression did not cause overt liver damage, except for a slight enlargement of the liver. However, the NS3/4A-transgenic mice displayed less spontaneously appearing intrahepatic inflammatory foci, which are commonly found in laboratory mice. Thus, expression of NS3/4A-protein may affect the distribution of immune cells within the liver.

The present studies demonstrate that NS3/4A-based genetic vaccines effectively prime humoral and cellular immune responses. Intra-hepatic expression of NS3/4A did not cause any spontaneous liver disease or overt pathology suggesting that it safely can be used in genetic vaccines. Thus, the NS3/4A gene can safely activate immune responses that are similar to those found in humans who can clear HCV. The NS3/4A should therefore be a potential vaccine candidate against chronic HCV infections.

Thesis: Development of vaccines and experimental models for chronic infections caused by the hepatitis C virus

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June 8th, 2004

Vertex Pharmaceuticals Announces Initiation of First Human Clinical Trial for VX-950, an Investigational Oral Protease Inhibitor for the Treatment of Hepatitis C

Source: PRNewswire

CAMBRIDGE, Mass-- Vertex Pharmaceuticals Incorporated (NASDAQ:VRTX) announced today the initiation of a Phase I clinical trial for VX-950, an investigational oral protease inhibitor for the treatment of hepatitis C virus (HCV) infection. The objective of this trial is to assess safety, tolerability and pharmacokinetics in escalating single doses of VX-950 in healthy volunteers. Approximately 35 healthy subjects will participate in the study, which is being conducted in Europe. Successful completion of the Phase I clinical trial will enable a first study of VX-950 in HCV-infected patients. Such a study is currently planned to start in the fourth quarter of 2004.

VX-950 is Vertex's lead oral HCV protease inhibitor and one of a new class of direct antivirals in development for the treatment of HCV. Preclinical studies have shown that VX-950 significantly reduces levels of HCV RNA in both an in vitro replicon system and infectious virus assays. At a scientific conference in October 2003, Vertex scientists reported that VX-950 reduced HCV RNA 10,000-fold (4 log₁₀) in nine days in an in vitro replicon assay. Preclinical pharmacokinetic studies have indicated that VX-950 is orally bioavailable and achieves excellent exposure in the liver, the target organ for HCV treatment. The initiation of clinical testing of VX-950 represents a first step towards establishing the safety and tolerability in humans.

"Preclinical data to date have indicated that direct antivirals such as VX-950 may represent a powerful new approach to the treatment of HCV infection," stated John J. Alam, M.D., Senior Vice President of Drug Evaluation and Approval at Vertex. "Initiation of human clinical trials for VX-950 reflects Vertex's commitment to leadership in the development and commercialization of novel antivirals for the treatment of HCV infection, and it is one of several important clinical milestones for Vertex's proprietary development programs in 2004."

Clinical Need and Market Opportunity in HCV Infection

Chronic hepatitis C virus (HCV) infection is a serious public health concern affecting approximately 2.7 million people in the United States. HCV causes inflammation of the liver, which may lead to fibrosis and cirrhosis, liver cancer, and ultimately, liver failure. Cirrhosis of the liver resulting from chronic HCV infection is the leading indication for liver transplantation in the U.S. Due to the asymptomatic nature of HCV infection, it often goes undetected for up to 20 years following initial infection. Worldwide, the disease strikes as many as 185 million people. Each year, 8,000 to 10,000 people in the U.S. die from complications of HCV.

The current standard of care in HCV treatment is a combination of weekly injections of pegylated interferon alpha (peg-IFN) and daily oral dosing of ribavirin. This combination therapy provides a sustained viral response for only 40 to 50 percent of patients chronically infected with genotype 1 HCV, the most difficult viral strain to treat and the most common form in the U.S.

Vertex's drug development portfolio includes two different approaches for advancing the future standard-of-care in HCV. In addition to VX-950, Vertex is developing merimepodib, an IMPDH inhibitor in combination with pegylated interferon alpha (peg-IFN) and ribavirin. Addition of merimepodib to standard therapy has the potential to enhance antiviral activity and improve clinical outcomes for a larger percentage of patients. Vertex owns worldwide development and commercialization rights for both merimepodib and VX-950.

About Vertex

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical partners. Vertex's product pipeline is principally focused on viral diseases, inflammation, autoimmune diseases and cancer. Vertex co-promotes the new HIV protease inhibitor, Lexiva(TM), with GlaxoSmithKline.

This press release may contain forward-looking statements, including statements that (i) successful completion of the Phase I trial would enable a first study to assess dosing in patients in the fourth quarter of 2004; (ii) preclinical testing results suggest that VX-950 may represent a powerful new approach in the treatment of HCV infection; and (iii) addition of merimepodib in combination therapy has the potential to improve clinical outcomes. While management makes its best efforts to be accurate in making forward-looking statements, such statements are subject to risks and uncertainties that could cause Vertex's actual results to vary materially. These risks and uncertainties include, among other things, the risks that clinical trials for merimepodib or VX-950 may not proceed as planned due to technical, scientific, supply or patient enrollment issues, that actual clinical studies of VX-950 will not reflect the results obtained in nonclinical testing, that clinical results may not demonstrate the value of combination therapies for HCV patients generally, and further clinical testing of merimepodib will not confirm its potential as an enhancement to combination therapy, and other risks listed under Risk Factors in Vertex's form 10-K filed with the Securities and Exchange Commission on March 15, 2004.

Lexiva(TM) is a registered trademark of the GlaxoSmithKline group of companies. Vertex's press releases are available at www.vrtx.com.

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Source: Vertex Pharmaceuticals Incorporated

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June 9th, 2004

Isis Pharmaceuticals (ISIS) Gains Full Ownership Of Orasense(TM) And HepaSense(TM) Subsidiaries And Eliminates Future Royalty Payments To Elan Corporation PLC (ELN)

Source: PRNewswire

CARLSBAD, Calif., -- Isis Pharmaceuticals, Inc. announced today that it has entered into an agreement with a subsidiary of Elan Corporation, plc, to acquire Elan's minority interest in Orasense and HepaSense, joint ventures arising out of prior collaborations between Isis and Elan. Through this acquisition, Isis has eliminated all future royalties to Elan related to the oral delivery platform developed within the Orasense collaboration and to ISIS 14803, Isis' antisense drug for the treatment of the hepatitis C virus, which is currently in Phase 2 clinical trials and was the focus of the HepaSense collaboration. As previously announced, Elan's participation in these collaborations concluded in January 2003 and November 2002, respectively.

In addition to eliminating all future royalty payments to Elan, the agreement allows Elan to transfer its shares of Isis Series B Preferred Stock to a third party. Upon transfer, the preferred stock will immediately convert to 1,055,502 shares of Isis common stock, eliminating the 5 percent in-kind dividend, thereby reducing future dilution of approximately 86,000 shares of Isis' common stock. Further, Elan has agreed to surrender its warrant to purchase 14,881 shares of Isis common stock to Isis for cancellation.

"We are extremely pleased to have completed this transaction as it allows us to recognize the full financial potential of our oral delivery platform and our proprietary drug to treat hepatitis C. In addition, it simplifies our capital structure and eliminates dividend accretion of approximately \$1.2 million between now and maturity in 2006 as a result of the early conversion of the Series B Preferred Stock," said B. Lynne Parshall, J.D., Executive Vice President and Chief Financial Officer of Isis. "This is the latest achievement in our ongoing efforts to further strengthen our financial position and streamline our balance sheet. As a result of these efforts over the past two years, we have retired more than \$125 million in high interest debt, eliminated a significant amount in future interest payments and reduced total potential dilution of our common stock by 2.2 million shares."

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 11 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases and cancer. Through its Ibis Therapeutics(R) program, Isis is developing a biosensor to identify infectious organisms, and discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,300 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com/>.

This press release includes forward-looking statements regarding our business, our financial position, the therapeutic and commercial potential of our technologies and products in development and the benefit we expect to receive from the transaction described herein. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as

Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this press release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended March 31, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

Ibis Therapeutics(R) is a registered trademark of Isis Pharmaceuticals, Inc.
Orasense(TM) and HepaSense(TM) are trademarks of Isis Pharmaceuticals, Inc.
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June 10th, 2004

Company to Issue Worldwide Alert to Hospitals About Dialysis Machines

Canadian Press

Chicago-based Baxter International is today expected to issue a global alert to hospitals using its hemodialysis machines - a response to concerns raised in British Columbia that the equipment may pose the risk of contamination between patients. Hundreds of British Columbia dialysis patients are being contacted regarding the small chance they have been put at risk of contracting a blood-borne illness like HIV or hepatitis B or C; some will have to take blood tests. The warning came after the discovery of blood inside tubing where it should not have been in a Baxter Aurora machine at Royal Jubilee Hospital in Victoria late last month.

Baxter spokesperson Cindy Resman said the company has "a huge team working on this" and will contact its customers around the world to ensure they are following the procedures in its manuals.

Michele Stewart, spokesperson for the provincial government, said Health Canada inspectors are interviewing company officials and will send a letter to all Canadian hospitals about the matter. Dr. Andeera Levin, medical director of the provincial renal agency, said there have been no cases of British Columbia dialysis patients contracting hepatitis in the past year. The patients are tested monthly for hepatitis B and about every six months for hepatitis C. While some dialysis patients have HIV and more have hepatitis, these patients do not use the same machines as uninfected patients.

The British Columbia Nurses' Union raised a red flag about Baxter last year because of lawsuits from deaths in Europe linked to Baxter products, union official Peggy Eburne said Thursday. Baxter spokesperson Deborah Spak said those problems related to faulty dialysers or filters and have nothing to do with the current machines. Baxter stopped making the faulty filters, closed the manufacturing facilities and settled with the families that sued, she said.

Sidney Pestka, M.D., Wins Sixteenth Annual Warren Alpert Foundation Prize

Source: PRNewswire

PISCATAWAY, N.J.-- Sidney Pestka, M.D., whose pioneering research made interferon therapy for hepatitis C and other viral diseases a reality, was named yesterday with two others as winner of the sixteenth annual Warren Alpert Foundation Scientific Prize.

The Foundation recognizes Dr. Pestka, Chairman and Chief Scientific Officer of PBL Biomedical Laboratories, for his seminal accomplishments in purifying, characterizing and cloning human interferon-alpha, or Hu-IFN-alpha, a virus-fighting substance produced by white blood cells. David V. Goeddel, Ph.D., founder and Chief Executive Officer of Tularik, Inc., and Charles Weissmann, M.D., Ph.D., the Institute of Neurology, University College London and Director of the Department of Infectology, Scripps Florida Research Institute, share the prize for crucial work in which they cloned Hu-IFN-alpha in the bacterium *E. coli* and demonstrated that biologically active interferon could be produced in large enough quantities to make it a practical treatment for disease. The Foundation will divide among the winners a \$150,000 award.

Interferon-alpha is the key component of the only known treatment regimen for hepatitis C, a viral disease of the liver spread by exposure to the blood of those already infected. Approximately 170 million persons suffer from chronic hepatitis C infection worldwide, and two to three million new cases are diagnosed each year. If untreated, chronic hepatitis C can lead to cirrhosis, and infection raises the risk of liver cancer 100-fold. But using a combined regimen of pegylated interferon-alpha and ribavirin, doctors now cure about 50 to 80 percent (depending on the viral strain) of chronically infected hepatitis patients, heading off permanent liver damage and cancer.

Interferon-alpha is used to treat several other viral diseases, including hepatitis B and human papillomavirus, or HPV, the most common sexually transmitted disease in the United States and the cause of most cervical cancer. Interferon is also used in the treatment of cancer. It has been shown to be effective in various forms of leukemia and in Kaposi's sarcoma, a cancer associated with HIV infection.

Scientists had noticed during the 1930s that viruses tend to strike one at a time. It is quite rare, for example, for a child to have measles and chickenpox simultaneously. Researchers explained this phenomenon by way of a theory of "viral interference," which proposed that cells exposed to a virus release some agent that protects the body from infection by other viruses. In 1957, scientists in London discovered a highly potent protein that played just such a protective role after viral infection, and they accordingly named it interferon.

The discovery of interferon, a natural cell product that acts against a wide range of viruses by protecting cells from infection and stimulating the immune system, was greeted with great excitement, and its clinical future seemed bright. However, cells produce interferon in miniscule amounts, and two decades' worth of attempts to purify and characterize the protein met with repeated failure.

Pestka first found he could greatly increase the interferon yield in his experiments by using white blood cells from leukemia patients, and then, after developing a new technique-reverse-phase

high-performance liquid chromatography, now used in biological laboratories throughout the world-he successfully purified ten unique interferon-alpha proteins in 1978.

Pestka's later collaborative work with Weissman (then at the University of Zurich) and Goeddel (then at Genentech) then led to the production, in bacteria, of as much human interferon-alpha per liter as could be made from the white blood cells of 100 donors. Moreover, the protein created in these experiments was potent enough to protect monkeys from otherwise deadly viral infections.

The translation of this research from the laboratory to the clinic was remarkably rapid. Recombinant interferon-alpha was first injected into a human patient in 1981, and the drug received FDA approval for the treatment of leukemia just five years later. Today, millions of patients throughout the world have received interferon-alpha for many conditions that were previously untreatable, and other potential uses for interferon continue to be explored in clinical trials and in basic research.

The Warren Alpert Foundation Scientific Prize

The Warren Alpert Foundation Scientific Prize is given each year for far-reaching scientific breakthroughs that have had a direct impact on the treatment of disease. Each year the Foundation receives 30 to 50 nominations for the Alpert Prize from scientific leaders worldwide. Prize recipients are selected by the Foundation's scientific advisory board, made up of internationally recognized biomedical scientists. See <http://www.hms.harvard.edu/fa/AlpertPrize/> for more information.

PBL Therapeutics

PBL Therapeutics is producing the next generation of interferon molecules -- Ultra Interferons(TM), which can be 20 to 30 times more potent than the interferons currently used in therapy. Equally significant, PBL Therapeutics has also developed its Sustained Release Protein Delivery (SuRe-PD(TM)) technology to deliver interferon directly to tumors and release the drug slowly over time. Together, Ultra Interferons(TM) and SuRe-PD(TM) are expected to enable PBL to develop more effective cancer treatments, with dramatically reduced side effects.

PBL Therapeutics, an emerging biotechnology company, has developed three technology platforms: (1) Using its drug discovery platform, PBL can identify a virtually unlimited number of interferon variants that are produced naturally in cancer cells. Selected variants under development are 20 to 30 times more effective than Alpha 2 interferon, the first and only interferon approved for cancer therapy. The Company screens these molecules to determine which "Ultra Interferon(TM)" possesses the preferred characteristics to treat the diseases of choice. (2) PBL then formulates the Ultra Interferon. using its Sustained Release Protein Delivery ("SuRe-PD(TM)") technology to deliver the interferon locally, and release it slowly over time. Together, these two technology platforms enable PBL Therapeutics to develop the most promising interferon molecule, and to maximize the effectiveness of this molecule through extended-release, localized delivery. (3) PBL Therapeutics' phosphorylation technology, used primarily to radiolabel monoclonal antibodies (MAbs), significantly improves upon the chemical labeling procedures currently used to target radiation to tumors. MAbs with genetically engineered phosphorylation sites facilitate the delivery of high-energy radioactivity to cancer cells. Phosphorylated MAbs retain higher activity and selectivity for tumor antigens and appear less immunogenic than MAbs radiolabeled through conventional chemical conjugation methods.

This technology complements the company's Ultra Interferons(TM), which stimulate expression of the tumor cell surface antigens that phosphorylated MAbs target.

Certain statements contained herein, including statements regarding development of the Company's products, services, markets, and future demands for the Company's products and services, and other statements regarding matters that are not historical facts, are forward-looking statements. Such forward-looking statements include risks and uncertainties; consequently, actual results may differ materially from those expressed or implied thereby.

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