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Therapeutics & Diagnostics
For the person in every patient

Prometheus Laboratories Launches PROCLIVITY 02, a Phase IV Multi-Center Study Comparing the Sequence of Proleukin® (Aldesleukin for Injection) and Yervoy® (Ipilimumab) in Patients with Metastatic Melanoma

PROCLIVITY℠ (**PRO**LEUKIN® **C**ombined with Ipi**LI**mumab, **V**emurafenib or other targeted agents **I**n the **T**reatment of Malignanc**Y**)

PROCLIVITY 01 trial passes initial safety milestone

San Diego, Calif., May 30, 2013 – Prometheus Laboratories Inc., a specialty pharmaceutical and diagnostic company, announces that PROCLIVITY02, a multi-center study comparing the sequence of Proleukin® (High Dose Interleukin-2 (HD IL-2)[1] followed by ipilimumab to the converse order, as therapy in patients with metastatic melanoma (mM) has Investigational Review Board approval and anticipates enrolling patients this summer. HD IL-2 therapy is administered in specialized hospitals as in-patient therapy and ipilimumab is administered via outpatient intravenous infusions. The study is being conducted in approximately 10-25 sites in the United States.

"Sequential treatment with two complementary immunotherapies may improve upon the clinical endpoints seen with HD IL-2 alone," stated Sapna Patel, BA, MD, co-principal investigator of the PROCLIVITY 02 trial, and Assistant Professor in the Department of Melanoma Medical Oncology in the Division of Cancer Medicine at the University of Texas M.D. Anderson Cancer Center in Houston, Texas. "By administering HD IL-2 followed by ipilimumab, or vice versa, we aim to assess whether the one-year survival is improved over historical controls, and to observe whether one sequence has an advantage over the other regarding practical administration and complete response rate," added Dr. Patel. Ipilimumab is a monoclonal antibody which blocks binding of the CTLA-4 immune checkpoint inhibitor to the CD28 receptor on T lymphocytes, thus removing a natural down regulator of the immune response. In combination with IL-2, the potent and specific stimulator of T cells, it is hypothesized that improved immune destruction of tumor cells might occur.

The randomized open-label, two-arm study is enrolling mM patients who are treatment-naïve or have previously received a single non-immunologic therapy. The trial will enroll approximately 120 patients, with 60 patients assigned to each treatment arm. Patients in Treatment Arm 1 will receive two courses (four cycles) of HD IL-2 followed by one course of the monoclonal antibody ipilimumab (3 mg/kg intravenously every 3 weeks, for a total of four doses). Patients in Treatment Arm 2 will receive the study drugs in the opposite sequence: one course (four doses) of ipilimumab followed by two courses (four cycles) of HD IL-2.

The study's primary endpoint is overall survival at one year in the protocol-defined population (i.e., those receiving more than 50% of the planned cycles of both study drugs). The complete responders in the protocol-defined population (Arm 1 + Arm 2) will be compared to that in a concurrent control population using data from the HD IL-2 Melanoma "SELECT" trial.[2] Similarly, both endpoints will be evaluated in the intent to treat population. Finally, the fraction of patients in each arm who receive $\geq$ 50% of the cycles of both drugs will be compared to each other.

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PROCLIVITY 01 Passes Safety Milestone
The PROCLIVITY 01 trial, which evaluates the combination of vemurafenib and HD IL-2 in metastatic melanoma, has passed its initial safety review by an independent Safety Monitoring Committee. The first 8 patients treated with vemurafenib and two cycles of HD IL-2 in this study showed no signs of synergistic or additive toxicity that would interrupt the trial or merit additional attention. The trial is currently open for enrollment in 15 sites.

For more information about PROCLIVITY 01, please visit:
http://www.cancer.gov/clinicaltrials/search/view?cdrid=740240&version=HealthProfessional&protocolsearchid=11587501

According to the American Cancer Society, an estimated 9,480 Americans will die of metastatic melanoma this year. When HD IL-2 is used to treat the disease, 16% of patients experience complete and partial responses, many of which are durable for years.[1] Although melanoma accounts for less than 5% of all skin cancer cases, it is responsible for the vast majority of skin cancer deaths.[3] "The lethality of melanoma and its rising incidence combined with the availability of several new therapies, have spurred investigation of sequential therapy," commented William H. Sharfman, MD, co-principal investigator of the PROCLIVITY 02 trial. "Up to now, HD IL-2 and ipilimumab, as single agents,have produced complete and durable responses in a small minority of patients.[4] If we can increase the population of durable responders by administering HD IL-2 sequentially with ipilimumab, without waiting for disease progression, we can begin to understand how to best employ therapy for metastatic melanoma in order to optimize patient outcomes," added Dr. Sharfman, who is Associate Professor of Oncology and Dermatology at Johns Hopkins Medicine in Baltimore, Md.

For more information on the PROCLIVITY clinical trial program, please call 858-587-4165 or visit www.clinicaltrials.gov (enter **aldesleukin** or **PROCLIVITY** in the "search" box on the top right). The PROCLIVITY clinical trial program is sponsored by Prometheus Laboratories Inc.

About Proleukin
Proleukin (aldesleukin) for injection is a human recombinant interleukin-2 for treatment in adults with metastatic melanoma and metastatic kidney cancer (mRCC). Proleukin therapy is a form of immunotherapy that enhances the body's natural immune system to help fight these types of cancer. Proleukin has been used for over 15 years in the treatment of metastatic melanoma and over 20 years in the treatment of metastatic kidney cancer (renal cell carcinoma). Complete plus partial response rates were 15% in mRCC patients and 16% in mM patients.

Important Safety Information
Therapy with Proleukin (aldesleukin) should be restricted to patients with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing. Extreme caution should be used in patients with a normal thallium stress test and a normal pulmonary function test who have a history of cardiac or pulmonary disease.

Proleukin should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

Proleukin administration has been associated with capillary leak syndrome (CLS), which is characterized by a loss of vascular tone and extravasation of plasma proteins and fluid into the extravascular space. CLS results in hypotension and reduced organ perfusion, which may be severe and can result in death. CLS may be associated with cardiac arrhythmias (supraventricular and ventricular), angina, myocardial

infarction, respiratory insufficiency requiring intubation, gastrointestinal bleeding or infarction, renal insufficiency, edema, and mental status changes.

Proleukin treatment is associated with impaired neutrophil function (reduced chemotaxis) and with an increased risk of disseminated infection, including sepsis and bacterial endocarditis. Consequently, preexisting bacterial infections should be adequately treated prior to initiation of Proleukin therapy. Patients with indwelling central lines are particularly at risk for infection with gram-positive microorganisms. Antibiotic prophylaxis with oxacillin, nafcillin, ciprofloxacin, or vancomycin has been associated with a reduced incidence of staphylococcal infections. Proleukin administration should be withheld in patients developing moderate to severe lethargy or somnolence; continued administration may result in coma.

About Interleukin-2
Interleukin-2 (IL-2) is a cytokine protein that occurs naturally in the body and plays an important role in activating the immune system. Proleukin is a recombinant version of IL-2. Proleukin possesses the same properties as naturally occurring IL-2 and when administered to patients with mM and mRCC activates the immune system to recognize and eliminate cancer cells.

Please see full Prescribing Information **for Proleukin.**

About Prometheus
Prometheus Laboratories Inc. is committed to improving lives through the development and commercialization of novel pharmaceutical and diagnostic products that enable physicians to provide greater individualized patient care. Prometheus is a leader in applying the principles of personalized medicine to the diagnosis and treatment of gastrointestinal diseases and is applying these principles to oncology. Its strategy includes the marketing and delivery of pharmaceutical products complemented by proprietary diagnostic testing services. By integrating therapeutics and diagnostics, Prometheus believes it can provide physicians with more targeted solutions to optimize care for their patients. Prometheus became part of Nestlé Health Science in July 2011. The corporate offices of Prometheus are located in San Diego, California. For more information about Prometheus, please visit www.prometheuslabs.com.

About Nestlé Health Science
Nestlé Health Science, a wholly-owned subsidiary of Nestlé, intends to spearhead the development of science-based personalised nutritional solutions. Building on its core HealthCare Nutrition business, the company has ambitions to address chronic conditions in the area of Gastrointestinal Health, Metabolic Health and Brain Health. Nestlé Health Science offers nutritional solutions for people with specific dietary needs related to illnesses, disease states or the special challenges of different life stages. Nestlé Health Science employs around 3,000 people worldwide and has its headquarters in Lutry, Switzerland.For more information, please visit www.nestlehealthscience.com.

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[1] PROLEUKIN Prescribing information. 600,000 International Units/kg (0.037 mg/kg) dose administered every 8 hours by a 15-minute intravenous infusion for a maximum of 14 doses. Following 9 days of rest, the schedule is repeated for another 14 doses, for a maximum of 28 doses per course, as tolerated. Page 15 (http://www.proleukin.com/assets/proleukin.pdf)

[2] IL-2 "SELECT" Tissue Collection Protocol in Patients with Advanced Melanoma. ClinicalTrials.gov. Bethesda, Md.: U.S. National Institutes of Health; 2011. http://clinicaltrials.gov/ct2/show/NCT01288963?term=SELECT&intr=aldesleukin&rank=2.

[3] American Cancer Society. *Cancer Facts & Figures 2013*. Atlanta, Ga.: American Cancer Society; 2013.

[4] Atkins MB, Lotze MT, Dutcher JP, et al. High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: analysis of 270 patients treated between 1985 and 1993. *J Clin Oncol* 1999; 17:2105-16.