# PROCLAIM[SM] Patient Registry Data Show Extension of Overall Survival Benefits Beyond Complete and Partial Responders in Metastatic Renal Cell Carcinoma Patients Treated with High-Dose Interleukin-2 (HD IL-2)

*Retrospective Analysis Demonstrates Survival Benefits for Patients with Stable and Progressive Disease after HD IL-2 in the Modern Era Suggesting Appropriate Drug Sequencing may Improve Outcomes*

**Chicago, IL, May 30, 2014 —** Prometheus Laboratories Inc. announced today that analysis of data from the PROCLAIM[SM] national patient registry retrospective cohort shows improved overall survival in metastatic RCC patients treated with high-dose Proleukin® (aldesleukin) in the tyrosine kinase inhibitor (TKI) era versus that previously published by the NCI in patients treated prior to 2005.[1] The survival benefit, well known in complete and partial responders to HD IL-2, was observed to extend to patients with stable or progressive disease after HD IL-2 when compared to results in patients receiving only TKI as published by the International Metastatic Renal-Cell Carcinoma Database Consortium (IMRCCDC).[2] The analysis, presented here today during a poster session at the 50th annual meeting of the American Society of Clinical Oncology (ASCO), also demonstrated a trend favoring patients receiving first-line versus second-line HD IL-2 immunotherapy, suggesting that patient selection and drug sequencing may yield better outcomes.[3]

"This multi-institutional study confirms several published single institution studies and Phase 2 data with axitinib and sorafenib demonstrating that serially-administered single agent TKIs appear to provide better survival after HD IL-2 administration,"[4,5,6] said James Lowder, MD, Senior Director of Oncology Clinical Development and Medical Affairs at Prometheus Laboratories Inc.. "In addition to validating that response to high-dose IL-2 is associated with prolonged survival, the PROCLAIM registry data show that stable disease and first-line use may positively impact survival in patients with metastatic renal cell carcinoma. If confirmed in the prospective registry patients, this would be instructive in understanding the optimal sequencing of IL-2 and targeted agents."

In a poster presentation entitled, "High Dose (HD) IL-2 for Metastatic Renal Cell Carcinoma (mRCC) in the Targeted Therapy Era: Extension of OS benefits beyond Complete Response (CR) and Partial Response (PR)," the PROCLAIM investigators presented an analysis of data collected retrospectively from 97 US patients with mRCC who received at least one dose of HD IL-2 and were followed for a median duration of 37.1 months. Of 77 patients with complete data, 28 were favorable, 55 intermediate and 1 poor prognosis using the IMRCCDC criteria. The median period of HD IL-2 cycles was 1.0 months (Range 0.03-11.8 months). The overall response rate (ORR) to IL-2 therapy was 22%, (8% complete responses (CR) and 14% partial responses (PR)) with an additional 24% of patients with stable disease (SD). Follow-up in this retrospective cohort after the initial HD IL-2 therapy was limited to survival. Further therapy of these patients was unknown, but presumed to have been TKI (vascular endothelial growth factor inhibitors or mammalian target of rapamycin inhibitors in patients who progressed. Of the 97 subjects, 39 were confirmed deceased and 58 were known to be alive; none were lost to follow-up. The median OS rate from the time of HD IL-2 administration was 51 months. This compares favorably with the median survival of 19 months observed in the pre-2006 NCI series of HD IL-2 alone, as well as, treatment of targeted therapy alone (IMRCCDC) of 19 months. The researchers reported a significant clinical benefit in patients with CR, PR, and stable disease (SD), none of whom have reached median OS; by comparison, median OS was 40.1 months in patients with progressive disease (PD).[3] In the past, it was believed that benefit from HD IL-2 was limited to the small proportion who achieved complete and partial responses. In the modern era, where a variety of effective targeted therapies exist which can be used as salvage, this benefit may extend to all patients.

In addition, median OS was 61.8 months for the 82 patients treated with first-line HD IL-2 therapy, compared to 48 months for the 15 patients who received IL-2 after prior TKI therapy. Although consistent with recently published data, interpretation of this finding is limited by the small number of patients receiving second-line

IL-2 and requires validation in the prospective cohort.[4] No deaths due to IL-2-related toxicity were reported in the retrospective PROCLAIM registry cohort.[3]

The PROCLAIM[SM] patient registry (www.proclaimregistry.com), an HD IL-2 observational database of melanoma and renal cell carcinoma patients covering more than 35 participating sites, consists of a retrospective cohort of patients treated between 2007 and 2012, as well as an ongoing prospective cohort of over 600 patients. Hypotheses such as patient selection characteristics and treatment sequences can be tested in the prospective cohort as their follow-up matures.[3]

"The survival in the PROCLAIM retrospective cohort exceeds the median overall survival in the studies that led to regulatory approval of IL-2 prior to the availability of TKI, suggesting that proper sequencing of IL-2 and targeted therapies may enable improved outcomes in appropriate patients," noted lead investigator Michael Morse, MD, MHS, Duke University School of Medicine. "As we continue to collect data in the prospective cohort, we hope to refine our understanding of which candidates are most likely to benefit from sequential therapy, and to use this knowledge to extend patients' lives."

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**About Proleukin**® (aldesleukin)
Proleukin for injection is a recombinant human interleukin-2 for treatment in adults with metastatic melanoma and metastatic kidney cancer. 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 10 years in the treatment of metastatic melanoma and for 20 years in the treatment of metastatic kidney cancer (renal cell carcinoma). For complete prescribing information, please visit www.proleukin.com

**Important Safety Information**
Therapy with Proleukin for injection 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 protein that occurs naturally in the body and plays an important role in activating the immune system. The immune system protects the body from foreign substances, cells, and tissues by responding to and resisting diseases. Proleukin therapy is a genetically engineered or recombinant version of IL-2. Proleukin therapy possesses the same properties as naturally occurring IL-2 and helps activate the immune system to recognize and eliminate certain kinds of cancer cells.

**About Prometheus Laboratories Inc.**
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 nutritional solutions. Building on its core HealthCare Nutrition business, the company has ambitions to address conditions in the area of Gastrointestinal Health, Metabolic Health and Brain Health. Nestlé Health Science employs around 3,500 people worldwide and has its headquarters in Vevey, Switzerland. For more information, please visit www.nestlehealthscience.com.

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[1] Klapper JA, Downey SG, Smith FO, et al. High dose interleukin-2 for the treatment of metastatic renal cell carcinoma: a retrospective analysis of response and survival in patients treated in the surgery branch at the National Cancer Institute between 1986 and 2006. *Cancer* 2008;113(2):293-301.

[2] Heng DCY, Xie W, Regan MM, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: a population-based study. *Lancet Oncol* 2013;14(2):141-148.

[3] Morse M, Wong MKK, Kaufman HL et al. High dose (HD) IL-2 for metastatic renal cell carcinoma (mRCC) in the targeted therapy era: extension of OS benefits beyond complete response (CR) and partial response (PR). Presented at the 50th annual meeting of the American Society of Clinical Oncology (ASCO), Chicago, IL, May 30, 2014. Abstract 4523

[4] Birkhäuser FD, Pantuck AJ, Rampersaud EN, et al. Salvage-targeted kidney cancer therapy in patients progressing on high-dose interleukin-2 immunotherapy: the UCLA experience. *Cancer J* 2013;19(3):189-96.

[5] Hanzly M, Aboumohamed A, Yarlagadda N, et al. High-dose Interleukin-2 Therapy for Metastatic Renal Cell Carcinoma: A Contemporary Experience. *Urology* 2014;83(5):1129-34.

[6] Rixe O, Bukowski RM, Michaelson MD, et al. Axitinib treatment in patients with cytokine-refractory metastatic renal-cell cancer: a phase II study. *Lancet Oncol* 2007;8(11):975-84.