RARITAN, N.J., Sept. 28, 2013 /PRNewswire/ -- Janssen Diagnostics, LLC announced today results from a study presented at the European Cancer Congress in Amsterdam, Netherlands, that demonstrated circulating tumor cell (CTC) enumeration using CELLSEARCH®, along with lactate dehydrogenase (LDH) as part of a composite biomarker panel, was an efficacy-response surrogate for survival in managing patients with metastatic castration-resistant prostate cancer (mCRPC). The results show mCRPC patients with greater than or equal to five CTCs and an abnormal LDH level at 12 weeks of treatment have a poorer prognosis than those with lower CTC counts and normal LDH values, with a one- and two-year survival probability of 25 percent and 2 percent compared to 82 percent and 46 percent, respectively. Findings suggest therapeutic alternatives should be considered for patients in the high-risk category at 12 weeks.

"This study is the first to demonstrate individual patient surrogacy for CTCs and provides a potential post-treatment outcome measure that may assist with managing an individual patient's disease," said lead study investigator Howard Scher, M.D., Genitourinary Oncology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center. "In cancer treatment it can be difficult to determine when a new therapy is needed for a patient. The ability to determine if a treatment is working for a patient, and switch as needed, could potentially have real clinical utility, especially for advanced disease such as metastatic castration-resistant prostate cancer."

CTC enumeration was included as an outcome measure in the multinational randomized, double-blind, placebo-controlled ZYTIGA® (abiraterone acetate) Phase 3 trial (COU-AA-301) in mCRPC patients previously treated with docetaxel. The primary endpoint was overall survival. The trial was conducted at 147 sites in 13 countries in North America, Europe, and Australia. Patients were randomized to receive ZYTIGA® 1000 mg daily or matched placebo. Both groups received prednisone 10 mg daily. Treatment was continued until disease progression based on PSA determinations, imaging, and/or clinical criteria, or until unacceptable toxicity.

One of the secondary objectives was the examination of CTC enumeration and other biomarkers as a potential surrogate for survival, recognizing that additional studies would be needed to confirm results. CTCs were measured at baseline and four, eight and 12 weeks. A trichotomous surrogate biomarker panel based on 12-week data categorized patients as low-risk (CTC less than or equal to 4), intermediate-risk (CTC greater than or equal to 5, LDH less than or equal to 250 IU/L) or high-risk (CTC greater than or equal to 5, LDH >250 IU/L). Individual level surrogacy, or clinical usefulness for treatment of individual patients, was assessed using Prentice criteria and trial level surrogacy by measuring the association between the treatment effect on the surrogate and survival within each country and randomly generated pseudo sub-studies. The Prentice criteria include the following: treatment must have a significant effect on the clinical end point, i.e., survival; treatment must have a significant effect on the proposed biomarker; the biomarker must have a significant impact on the clinical end point; and the full effect of treatment on the clinical end point must be captured by the biomarker.

"These data reinforce Janssen's commitment to patients in need, with the goal of helping health care professionals determine the right therapy at the right time," said Robert McCormack, Ph.D., Head of Technology Innovation at Janssen Diagnostics, LLC. "At the individual patient level, these results indicate CTCs may be a useful indicator of therapy effectiveness in men with metastatic castration-resistant prostate cancer. We are continuing to study CTCs at both the individual patient and larger trial level, and look forward to sharing our findings when the data mature."

Complete biomarker data at 12 weeks were available from 711 of 1195 patients; some study sites/countries were unable to assess CTCs. All Prentice criteria were satisfied at the individual level: survival differed between the ZYTIGA® and placebo arms (p=0.034); surrogate distribution differed by treatment (p<0.001); the surrogate had strong discriminatory power to distinguish low- and high-risk patients (concordance probability estimate [CPE] = 0.79); and the treatment effect on survival was explained by the surrogate. There was only a weak association between the surrogate and survival at the trial level, potentially related to the small sample sizes of the groups studied.

The CELLSEARCH® system is the only CTC test that has obtained U.S. Food and Drug Administration (FDA) 510(k) clearance for aiding in the monitoring of patients with metastatic breast, colorectal or prostate cancer. In addition to its clearance in the U.S. and approval in China
for the monitoring of patients with metastatic breast cancer, CELLSEARCH
®
fulfills the requirements for CE marking in the European Union (EU). CE marking indicates compliance with EU legislation of a product, wherever in the world manufactured, and enables

its free movement within the European market.

About Circulating Tumor Cells Circulating tumor cells are cancer cells that have detached from the tumor and are found at extremely low levels in the bloodstream. The value of capturing and counting CTCs is evolving as more research data is gathered about the utility of these markers in monitoring disease progression and potentially guiding personalized cancer therapy.

About Janssen Diagnostics Janssen Diagnostics is the center of excellence in specialized diagnostics development, an important role within the global Janssen pharmaceutical companies. In 1953, founder Dr. Paul Janssen championed an unwavering focus on pharmacological and medical research with a singular objective to improve quality of life by developing medicines that addressed unmet medical needs.

The Janssen Diagnostics team shares that same vision and is dedicated to improving patients' lives, one by one, by making truly personalized care the cornerstone of our healthcare system. Our goal is to influence current thinking beyond drug treatment and develop as a solutions provider. The Janssen legacy of excellence will continue to inspire innovation utilizing real-world data and enable us to reach our goal in developing care solutions that cater to the needs of each individual patient.

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