Pfizer Logo

First Positive Phase 3 Results In Adjuvant Setting For Renal Cell Carcinoma Show SUTENT® (sunitinib) Extended Disease Free Survival After Surgical Removal

Sunday, October 09, 2016 - 10:15pm

Late-breaking data to be presented at the ESMO 2016 Congress and Published in The New England Journal of Medicine

Pfizer Inc. (NYSE:PFE) today announced results from the Phase 3 S-TRAC clinical trial (Sunitinib Trial as Adjuvant Treatment of Renal Cancer) investigating SUTENT® (sunitinib) as adjuvant therapy. The trial showed SUTENT extended disease-free survival (DFS) by more than one year versus placebo in patients who were at high risk for recurrence after surgical resection of renal cell carcinoma (RCC) (HR 0.761; P=0.030 [95% CI: 0.594-0.975]). These results will be presented today during a Presidential Symposium (Abstract #LBA11_PR) at the ESMO 2016 Congress, the annual meeting of the European Society for Medical Oncology being held in Copenhagen, Denmark. The results have also been published online by *The New England Journal of Medicine*.

Adjuvant therapies are treatments that can be given to reduce the likelihood of the cancer returning after initial treatment such as surgery.

“We are encouraged by the S-TRAC results because this is the first clinical trial to show increased disease-free survival in the adjuvant setting for RCC,” said lead investigator Alain Ravaud, M.D., Ph.D., CHU de Bordeaux Hôpital Saint André. “These data are promising for RCC patients as there are no effective treatments currently available in this setting.”

The results from the S-TRAC trial showed that after one year of treatment, the median time until disease recurrence in participants treated with SUTENT after surgery was 6.8 years compared with 5.6 years for patients treated with placebo as assessed by independent central review, resulting in an overall risk reduction of 24 percent. At the time of the analysis, overall survival (OS) data was immature.

Based on the results of S-TRAC, Pfizer is in discussions with global regulatory authorities to determine potential next steps.

“For the past 10 years, Pfizer has been a leader in developing new treatments for patients with kidney cancer, and SUTENT has been the most widely prescribed first line treatment for thousands of patients with advanced RCC around the world,” said Mace Rothenberg, MD, Chief Development Officer, Oncology, Pfizer Global Product Development. “The results of S-TRAC suggest that SUTENT has the potential to extend this benefit by reducing the risk of recurrence in patients who have undergone complete surgical removal of their kidney cancer and are at high risk of cancer recurrence.”

The adverse events seen in the trial were consistent with SUTENT's known safety profile. The most common adverse reactions (>20%) are fatigue, asthenia, and fever. Grade ?3 adverse events were more frequent with SUTENT (62.1%) vs. placebo (21.1%). No deaths occurred due to treatment toxicity.

SUTENT is an oral cancer medication that was first approved in the United States in 2006 for the treatment of advanced RCC. It is currently approved in 119 countries.i Worldwide more than 250,000 patients across diagnoses have been treated with SUTENT in its approved indications of advanced RCC, imatinib-resistant or -intolerant gastrointestinal stromal tumors (GIST) and advanced pancreatic neuroendocrine tumors (pNET).ii SUTENT is not approved in the adjuvant setting.

About Renal Cell Carcinoma (RCC)

Each year, approximately 338,000 new cases of kidney cancer are diagnosed worldwide, representing approximately 2-3 percent of all cancers.iii Renal cell carcinoma (RCC) is the most common type of kidney cancer, accounting for around 90 percent of cases.iv

About S-TRAC

The S-TRAC trial was a randomized double-blind Phase 3 trial of adjuvant SUTENT vs. placebo in 615 patients with local, resected RCC at high risk of recurrence. Patients received 50 mg/d of SUTENT or placebo in a four weeks on, two weeks off schedule for one year until disease recurrence, occurrence of secondary malignancy, significant toxicity or consent withdrawal. The primary objective was to demonstrate an improvement in DFS by blinded independent central radiologic review. DFS was defined as the time interval from the date of randomization to the first date of recurrence or the occurrence of a secondary malignancy or death. Recurrence referred to relapse of the primary tumor locally or at metastatic sites. The S-TRAC trial has two cohorts: Global and China. These results are from the Global cohort only. Results from the China cohort are not yet mature and will be reported at a later date.

About SUTENT® (sunitinib malate)

SUTENT is an oral multi-kinase inhibitor that works by blocking multiple molecular targets implicated in the growth, proliferation and spread of cancer. Two important SUTENT targets, vascular endothelial growth factor receptor (VEGFR) and platelet-derived growth factor receptor (PDGFR) are expressed by many types of solid tumors and are thought to play a crucial role in angiogenesis, the process by which tumors acquire blood vessels, oxygen and nutrients needed for growth. SUTENT also inhibits other targets important to tumor growth, including KIT, FLT3 and RET.

SUTENT is indicated for the treatment of advanced renal cell carcinoma (RCC), gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate, and progressive, well-differentiated pancreatic neuroendocrine tumors (pNET) in patients with unresectable locally advanced or metastatic disease.

SUTENT Important Safety Information

Boxed Warning/Hepatotoxicity: **Hepatotoxicity has been observed in clinical trials and post-marketing experience. This hepatotoxicity may be severe, and deaths have been reported.** Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. SUTENT should be interrupted for Grade 3 or 4 drug-related hepatic adverse events and discontinued if there is no resolution. Do not restart SUTENT if patients subsequently experience severe changes in liver function tests or have other signs and symptoms of liver failure.

Pregnancy: Women of childbearing potential should be advised of the potential hazard to the fetus and to avoid becoming pregnant.

Nursing mothers: Given the potential for serious adverse reactions (ARs) in nursing infants, a decision should be made whether to discontinue nursing or SUTENT.

Cardiovascular events: Cardiovascular events, including heart failure, cardiomyopathy, myocardial ischemia, and myocardial infarction, some of which were fatal, have been reported. Use SUTENT with caution in patients who are at risk for, or who have a history of, these events. Monitor patients for signs and symptoms of congestive heart failure (CHF) and, in the presence of clinical manifestations, discontinuation is recommended. Patients who presented with cardiac events, pulmonary embolism, or cerebrovascular events within the previous 12 months were excluded from clinical studies.

QT interval prolongation and Torsades de Pointes: SUTENT has been shown to prolong QT interval in a dose-dependent manner, which may lead to an increased risk for ventricular arrhythmias including Torsades de Pointes, which has been seen in <0.1% of patients. Monitoring with on-treatment electrocardiograms and electrolytes should be considered.

Hypertension: Hypertension may occur. Monitor blood pressure and treat as needed with standard antihypertensive therapy. In cases of severe hypertension, temporary suspension of SUTENT is recommended until hypertension is controlled.

Reversible posterior leukoencephalopathy syndrome (RPLS): There have been (<1%) reports, some fatal, of subjects presenting with seizures and radiological evidence of RPLS.

Hemorrhagic events: Hemorrhagic events, including tumor-related hemorrhage such as pulmonary hemorrhage, have occurred. Some of these events were fatal. Perform serial complete blood counts (CBCs) and physical examinations.

Tumor lysis syndrome (TLS): Cases of TLS have been reported primarily in patients with high tumor burden. Monitor these patients closely and treat as clinically indicated.

Thrombotic microangiopathy (TMA): TMA, including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome, sometimes leading to renal failure or a fatal outcome, has been reported in patients who received SUTENT as monotherapy and in combination with bevacizumab. Discontinue SUTENT in patients developing TMA. Reversal of the effects of TMA has been observed after treatment was discontinued.

Proteinuria: Proteinuria and nephrotic syndrome have been reported. Some of these cases have resulted in renal failure and fatal outcomes. Perform baseline and periodic urinalysis during treatment, with follow-up measurement of 24-hour urine protein as clinically indicated. Interrupt SUTENT and dose reduce if 24-hour urine protein is ?3 g; discontinue SUTENT in cases of nephrotic syndrome or repeat episodes of urine protein ?3 g despite dose reductions.

Dermatologic toxicities: Severe cutaneous reactions have been reported, including cases of erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), some of which were fatal. If signs or symptoms of EM, SJS, or TEN are present, SUTENT treatment should be discontinued. If a diagnosis of SJS or TEN is suspected, treatment must not be re-started. Necrotizing fasciitis, including fatal cases, has been reported, including of the perineum and secondary to fistula formation. Discontinue SUTENT in patients who develop necrotizing fasciitis.

Thyroid dysfunction: Thyroid dysfunction may occur. Monitor thyroid function in patients with signs and/or symptoms of thyroid dysfunction, including hypothyroidism, hyperthyroidism, and thyroiditis, and treat per standard medical practice.

Hypoglycemia: SUTENT has been associated with symptomatic hypoglycemia, which may result in loss of consciousness or require hospitalization. Reductions in blood glucose levels may be worse in patients with diabetes. Check blood glucose levels regularly during and after discontinuation of SUTENT. Assess whether anti-diabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

Osteonecrosis of the jaw (ONJ): ONJ has been reported. Consider preventive dentistry prior to treatment with SUTENT. If possible, avoid invasive dental procedures, particularly in patients receiving bisphosphonates.

Wound healing: Cases of impaired wound healing have been reported. Temporary interruption of therapy with SUTENT is recommended in patients undergoing major surgical procedures.

Adrenal function: Adrenal hemorrhage was observed in animal studies. Monitor adrenal function in case of stress such as surgery, trauma, or severe infection.

Laboratory tests: CBCs with platelet count and serum chemistries including phosphate should be performed at the beginning of each treatment cycle for patients receiving treatment with SUTENT.

CYP3A4 coadministration: Dose adjustments are recommended when SUTENT is administered with CYP3A4 inhibitors or inducers. During treatment with SUTENT, patients should not drink grapefruit juice, eat grapefruit, or take St John's Wort.

Most common ARs & most common grade 3/4 ARs (advanced RCC): The most common ARs occurring in ?20% of patients receiving SUTENT for treatment-naïve metastatic RCC (all grades, vs IFN?) were diarrhea (66% vs 21%), fatigue (62% vs 56%), nausea (58% vs 41%), anorexia (48% vs 42%), altered taste (47% vs 15%), mucositis/stomatitis (47% vs 5%), pain in extremity/limb discomfort (40% vs 30%), vomiting (39% vs 17%), bleeding, all sites (37% vs 10%), hypertension (34% vs 4%), dyspepsia (34% vs 4%), arthralgia (30% vs 19%), abdominal pain (30% vs 12%), rash (29% vs 11%), hand-foot syndrome (29% vs 1%), back pain (28% vs 14%), cough (27% vs 14%), asthenia (26% vs 22%), dyspnea (26% vs 20%), skin discoloration/yellow skin (25% vs 0%), peripheral edema (24% vs 5%), headache (23% vs 19%), constipation (23% vs 14%), dry skin (23% vs 7%), fever (22% vs 37%), and hair color changes (20% vs <1%). The most common grade 3/4 ARs (occurring in ?5% of patients with RCC receiving SUTENT vs IFN?) were fatigue (15% vs 15%), hypertension (13% vs <1%), asthenia (11% vs 6%), diarrhea (10% vs <1%), hand-foot syndrome (8% vs 0%), dyspnea (6% vs 4%), nausea (6% vs 2%), back pain (5% vs 2%), pain in extremity/limb discomfort (5% vs 2%), vomiting (5% vs 1%), and abdominal pain (5% vs 1%).

Most common grade 3/4 lab abnormalities (advanced RCC): The most common grade 3/4 lab abnormalities (occurring in ?5% of patients with RCC receiving SUTENT vs IFN?) included lymphocytes (18% vs 26%), lipase (18% vs 8%), neutrophils (17% vs 9%), uric acid (14% vs 8%), platelets (9% vs 1%), hemoglobin (8% vs 5%), sodium decreased (8% vs 4%), leukocytes (8% vs 2%), glucose increased (6% vs 6%), phosphorus (6% vs 6%), and amylase (6% vs 3%).

Most common ARs & most common grade 3/4 ARs (imatinib-resistant or -intolerant GIST): The most common ARs occurring in ?20% of patients with GIST and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (40% vs 27%), anorexia (33% vs 29%), skin discoloration (30% vs 23%), mucositis/stomatitis (29% vs 18%), asthenia (22% vs 11%), altered taste (21% vs 12%), and constipation (20% vs 14%). The most common grade 3/4 ARs (occurring in ?4% of patients with GIST receiving SUTENT vs

placebo) were asthenia (5% vs 3%), hand-foot syndrome (4% vs 3%), diarrhea (4% vs 0%), and hypertension (4% vs 0%).

Most common grade 3/4 lab abnormalities (imatinib-resistant or -intolerant GIST): The most common grade 3/4 lab abnormalities (occurring in ?5% of patients with GIST receiving SUTENT vs placebo) included lipase (10% vs 7%), neutrophils (10% vs 0%), amylase (5% vs 3%), and platelets (5% vs 0%).

Most common ARs & most common grade 3/4 ARs (advanced pNET): The most common ARs occurring in ?20% of patients with advanced pNET and more commonly with SUTENT than placebo (all grades, vs placebo) were diarrhea (59% vs 39%), stomatitis/oral syndromes (48% vs 18%), nausea (45% vs 29%), abdominal pain (39% vs 34%), vomiting (34% vs 31%), asthenia (34% vs 27%), fatigue (33% vs 27%), hair color changes (29% vs 1%), hypertension (27% vs 5%), hand-foot syndrome (23% vs 2%), bleeding events (22% vs 10%), epistaxis (21% vs 5%), and dysgeusia (21% vs 5%). The most commonly reported grade 3/4 ARs (occurring in ?5% of patients with advanced pNET receiving SUTENT vs placebo) were hypertension (10% vs 1%), hand-foot syndrome (6% vs 0%), stomatitis/oral syndromes (6% vs 0%), abdominal pain (5% vs 10%), fatigue (5% vs 9%), asthenia (5% vs 4%), and diarrhea (5% vs 2%).

Most common grade 3/4 lab abnormalities (advanced pNET): The most common grade 3/4 lab abnormalities (occurring in ?5% of patients with advanced pNET receiving SUTENT vs placebo) included decreased neutrophils (16% vs 0%), increased glucose (12% vs 18%), increased alkaline phosphatase (10% vs 11%), decreased phosphorus (7% vs 5%), decreased lymphocytes (7% vs 4%), increased creatinine (5% vs 5%), increased lipase (5% vs 4%), increased AST (5% vs 3%), and decreased platelets (5% vs 0%).

Please see ***full Prescribing Information***, **including BOXED WARNING and Medication Guide, for SUTENT® (sunitinib malate)**.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on those living with cancer. As a leader in oncology speeding cures and accessible breakthrough medicines to patients, Pfizer Oncology is helping to redefine life with cancer. Our strong pipeline of biologics, small molecules and immunotherapies is one of the most robust in the industry, and is studied with precise focus on identifying and translating the best scientific breakthroughs into clinical application for patients across a wide range of cancers. By working collaboratively with academic institutions, individual researchers, cooperative research groups, governments and licensing partners, Pfizer Oncology strives to cure or control cancer with its breakthrough medicines. Because Pfizer Oncology knows that success in oncology is not measured solely by the medicines you manufacture, but rather by the meaningful partnerships you make to have a more positive impact on people’s lives.

Pfizer Inc.: Working together for a healthier worldTM

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of healthcare products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer healthcare products. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. For more information, please visit us at www.pfizer.com. In addition,

to learn more, follow us on Twitter at @Pfizer and@Pfizer_News, LinkedIn, YouTube, and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of October 10, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about SUTENT and a potential new indication for SUTENT for the treatment of RCC in the adjuvant setting (the "potential indication"), including their potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development, including the ability to meet any anticipated regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; whether and when any supplemental new drug applications may be filed in any jurisdictions for the potential indication; whether and when any such applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of SUTENT; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

---

i Pfizer Data on File.
ii Pfizer Data on File.
iii Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM.GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 Lyon, France: International Agency for Research on Cancer; 2010. Available at: http://globocan.iarc.fr. Accessed September 2016.
iv What is Kidney Cancer. James Whale Fund for Kidney Cancer. Available at: http://www.jameswhalefund.org/kidneycancer/what-is-kidney-cancer/. Accessed September 2016.

Media: U.S. Sally Beatty, 212-733-6566 or Europe Lisa O'Neill, +44 1737 331536 or Investors: Ryan Crowe, 212-733-8160