Pfizer Logo

Pfizer Announces Outcome of FDA Advisory Committee Meeting for SUTENT® in Patients at High Risk of Recurrent Renal Cell Carcinoma after Surgery

Tuesday, September 19, 2017 - 09:15am

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration's (FDA) Oncologic Drug Advisory Committee (ODAC) voted 6 in favor and 6 against the benefit-risk profile for SUTENT® (sunitinib) as adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma (RCC) after nephrectomy (surgical removal of the cancer-containing kidney). The role of the Advisory Committee is to provide recommendations to the FDA. The ODAC discussions were based on the supplemental New Drug Application (sNDA) currently under review by the FDA. The FDA decision on whether or not to approve the sNDA is anticipated by January 2018.

Approximately 75 percent of patients with clear cell RCC are non-metastatic, and 70-80 percent will have a nephrectomy with curative intent, or surgical removal of the tumor.1 High-risk patients represent approximately 15 percent of all patients with primary resected RCC and approximately 60 percent of these high-risk patients will have recurrence and develop metastatic disease within five years.2 The current treatment is surgery followed by observation. This treatment is suboptimal for patients at high risk of recurrence.

"We are encouraged by today's productive discussion and look forward to working with the FDA over the next few weeks as they incorporate today's discussion into their review and decision regarding SUTENT in this patient population," said Mace Rothenberg, MD, Chief Development Officer, Oncology, Pfizer Global Product Development. "SUTENT has long been a standard of care for the treatment of advanced RCC and we believe that this potential benefit can be extended into patients with high-risk of RCC recurrence, as demonstrated in the S-TRAC trial."

The sNDA under review by the FDA is based on results from the S-TRAC trial, a randomized double-blind Phase 3 trial of adjuvant SUTENT vs. placebo in 615 patients with locoregional, resected RCC at high risk of recurrence. The study met its primary endpoint of improving disease-free survival (DFS), and the results were published by The New England Journal of Medicine in October 2016.

SUTENT was first approved in the United States in 2006 for the treatment of advanced RCC, where it is the most widely prescribed first-line treatment. Now approved in 119 countries,3 more than 350,000 patients 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).4 Use of SUTENT is not approved in the adjuvant setting. SUTENT is supported by an extensive body of evidence in scientific literature, including more than 440 publications.

The ODAC is an independent panel of experts that evaluates data concerning the efficacy and safety of marketed and investigational cancer treatments and makes recommendations to the FDA. Its vote is not binding, but is considered by the FDA in its decision making process.

As a leader in the treatment of advanced RCC, Pfizer is dedicated to meeting the unmet needs of these patients and advancing the science of RCC through research into established and novel compounds. Our near term areas of focus include expanding access of our marketed products, exploration of biomarkers to better personalize therapy and immunotherapy combinations.

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 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) at www.SUTENT.com.

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, one of the most robust in the industry, 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 world®

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, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com.In addition, to learn more, please visit us on www.Pfizer.com and 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 September 19, 2017. 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 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 other jurisdictions for the potential indication; whether and when the sNDA or any such other applications that may be pending or filed for the potential indication may be approved by the FDA or other regulatory authorities, respectively, 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, including for the potential indication; 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, 2016 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.

1 Based on comparison between 2015 Swedish population study (76%), Navigant interviews (95%), and Quant Pulse (79%). 2018-2022.

2 Wheler J, Johnson M, Seidman A. Adjuvant therapy with aromatase inhibitors for postmenopausal women with early breast cancer: evidence and ongoing controversy. Semin Oncol; 2006; 33(6): 672-80.

3 Pfizer Data on File.

4 Based on comparison between 2015 Swedish population study (76%), Navigant interviews (95%), and Quant Pulse (79%). 2018-2022.

Pfizer Inc. Media: Sally Beatty, 212-733-6566 or Investors: Ryan Crowe, 212-733-8160