Pfizer Receives FDA Approval for SUTENT® (sunitinib malate) as First and Only Adjuvant Treatment for Adult Patients at High Risk of Recurrent Renal Cell Carcinoma

Thursday, November 16, 2017 - 11:58am

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration has approved a new indication expanding the use of SUTENT® (sunitinib malate) to include the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma (RCC) following nephrectomy (surgical removal of the cancerous kidney). The approval was based on results from the S-TRAC trial that demonstrated a significant reduction in the risk of a disease-free survival (DFS) event (defined as the interval between randomization and tumor recurrence, or secondary primary cancer or death from any cause) for patients at high risk of RCC recurrence who received SUTENT compared to placebo in the adjuvant setting.

SUTENT has been a standard of care for the treatment of advanced RCC since it was approved more than a decade ago, and is now the first approved adjuvant treatment option for certain patients at high risk of recurrent RCC - the most common type of kidney cancer. The current treatment approach for RCC patients is surgery followed by observation, which is suboptimal for patients at high risk of recurrence.

“Today’s approval marks an important step forward for the treatment of adult patients who are at high risk of their renal cell carcinoma returning after surgery,” said Liz Barrett, global president and general manager, Pfizer Oncology. “Pfizer has been dedicated to advancing the science of RCC treatment for over a decade, and we are pleased to see

this commitment continue to translate into meaningful options for patients.”

The S-TRAC trial was a multicenter, international, randomized, double-blind, placebo-controlled Phase 3 trial of SUTENT versus placebo in 615 patients with clear cell histology and high risk of recurrent RCC following nephrectomy. The study met its primary endpoint of improving DFS and the results were published by The New England Journal of Medicine in October 2016.

“Some patients who have undergone surgery for locally advanced RCC are at high risk of recurrence and often fear their disease returning,” said Daniel George, MD, study investigator and medical oncologist at Duke University Medical Center. “This adjuvant therapy is the first-of-its-kind and a remarkable clinical development for these patients who before today, have been restricted to a wait and see approach.”

In the S-TRAC trial, the Hazard Ratio (HR) was 0.76 (95% CI: 0.59, 0.98) with a 2-sided p-value=0.03 in favor of SUTENT, representing a statistically significant 24% relative reduction in the risk of a DFS event. The median DFS was 6.8 years (95% CI: 5.8, not reached [NR]) in the SUTENT arm compared with 5.6 years (95% CI: 3.8, 6.6) in the placebo arm. At five years, the DFS rate for patients receiving SUTENT was 59.3% and 51.3% for placebo. This represents a persistent 8% absolute benefit.

No new safety signals were identified in the S-TRAC trial. The most common adverse reactions occurring in ≥20% of patients receiving SUTENT for adjuvant treatment of RCC (all grades) were mucositis/stomatitis (61%), fatigue/asthenia (57%), diarrhea (57%), hand-foot syndrome (50%), hypertension (39%), altered taste (38%), nausea (34%), dyspepsia (27%), abdominal pain (25%), rash (24%), hypothyroidism/TSH increased (24%), bleeding events, all sites (24%), and hair color changes (22%). The prescribing information for SUTENT also includes a boxed warning for hepatotoxicity and notes the following warnings and precautions: cardiovascular events; QT Interval Prolongation and Torsades de Pointes; hypertension; hemorrhagic events and viscus perforation; Tumor Lysis Syndrome (TLS); thrombotic microangiopathy (TMA); proteinuria; dermatologic toxicities; thyroid dysfunction; hypoglycemia; osteonecrosis of the jaw (ONJ); wound healing; and embryo-fetal toxicity. For more information, including Boxed Warning, please see the Important Safety Information for SUTENT below.

SUTENT Important Safety Information

Hepatotoxicity has been observed in clinical trials and postmarketing experience. Hepatotoxicity may be severe, and in some cases fatal. Monitor hepatic function and interrupt, reduce, or discontinue dosing as recommended.

Fatal liver failure has been observed. Monitor liver function tests before initiation of treatment, during each cycle of treatment, and as clinically indicated. Interrupt SUTENT for Grade 3 or 4 drug-related hepatic adverse reactions and discontinue if there is no resolution. Do not restart SUTENT if patients subsequently experience severe changes in liver function tests or have signs and symptoms of liver failure.

Cardiovascular events, including myocardial ischemia, myocardial infarction, left ventricular ejection fraction declines to below the lower limit of normal and cardiac failure including death have occurred. Monitor patients for signs and symptoms of congestive heart failure. Discontinue SUTENT for clinical manifestations of congestive heart failure. In patients without cardiac risk factors, a baseline evaluation of ejection fraction should be considered. Baseline and periodic evaluations of left ventricular ejection fraction should also be considered while these patients are receiving SUTENT.

SUTENT can cause **QT Prolongation** 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. Monitor patients that are at a higher risk for developing QT interval prolongation, including those with a history of QT interval prolongation, patients who are taking antiarrhythmics, or patients with relevant pre-existing cardiac disease, bradycardia, or electrolyte disturbances. Consider monitoring of electrocardiograms and electrolytes. Concomitant treatment with strong CYP3A4 inhibitors may increase sunitinib plasma concentrations and dose reduction of SUTENT should be considered.

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.

Hemorrhagic events, including tumor-related hemorrhage, and viscus perforation (both with fatal events) have occurred. These events may occur suddenly, and in the case of pulmonary tumors, may present as severe and life-threatening hemoptysis or pulmonary hemorrhage. Perform serial complete blood counts (CBCs) and physical examinations.

Cases of **tumor lysis syndrome** (TLS) (some fatal) have been reported. Patients generally at risk of TLS are those with high tumor burden prior to treatment. Monitor these patients closely and treat as clinically indicated.

Thrombotic microangiopathy (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 and nephrotic syndrome have been reported. Some of these cases have resulted in renal failure and fatal outcomes. Monitor patients for the development or worsening of proteinuria. Perform baseline and periodic urinalysis during treatment, with follow-up measurement of 24-hour urine protein as clinically indicated. Interrupt treatment for 24-hour urine protein ≥3 grams. Discontinue for repeat episodes of protein ≥3 grams despite dose reductions or nephrotic syndrome.

Dermatologic toxicities: Severe cutaneous reactions have been reported, including cases of necrotizing fasciitis, 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, discontinue SUTENT treatment. 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 may occur**.** Monitor thyroid function in patients with signs and/or symptoms suggestive of thyroid dysfunction, including hypothyroidism, hyperthyroidism, and thyroiditis, and treat per standard medical practice.

Hypoglycemia may occur. SUTENT can result in symptomatic hypoglycemia, which may lead to a 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 treatment with SUTENT. Assess if antidiabetic drug dosage needs to be adjusted to minimize the risk of hypoglycemia.

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

Impaired wound healing has occurred with SUTENT. Temporary interruption of therapy with SUTENT is recommended in patients undergoing major surgical procedures. There is limited clinical experience regarding the timing of reinitiation of therapy following major surgical intervention. Therefore, the decision to resume SUTENT therapy following a major surgical intervention should be based upon clinical judgment of recovery from surgery.

Embryo fetal toxicity and reproductive potential

Females - SUTENT can cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with SUTENT and for 4 weeks following the final dose

Males - Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment with SUTENT and for 7 weeks after the last dose

Male and female infertility - based on findings in animals, male and female fertility may be compromised by treatment with SUTENT

Lactation: Because of the potential for serious adverse reactions in breastfed infants from SUTENT, advise a lactating woman not to breastfeed during treatment with SUTENT and for at least 4 weeks after the last dose.

Venous thromboembolic events: In patients treated with SUTENT (N=7527) for GIST, advanced RCC, adjuvant treatment of RCC and pNET, 3.5% of patients experienced a venous thromboembolic event; 2.2% Grade 3-4.

There have been (<1%) reports, some fatal, of subjects presenting with seizures and radiological evidence of reversible posterior leukoencephalopathy syndrome (RPLS). Patients with seizures and signs/symptoms consistent with RPLS, such as hypertension, headache, decreased alertness, altered mental functioning, and visual loss, including cortical blindness, should be controlled with medical management including control of hypertension. Temporary suspension of SUTENT is recommended; following resolution, treatment may be resumed at the discretion of the treating healthcare provider.

Pancreatic function: In a trial of patients receiving adjuvant treatment for RCC, 1 patient (<1%) on SUTENT and none on placebo experienced pancreatitis.

CYP3A4 inhibitors and inducers: 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 (adjuvant RCC): The most common ARs reported in ≥20% of patients receiving SUTENT for adjuvant treatment of RCC and more commonly than in patients given placebo (all grades, vs placebo) were mucositis/stomatitis (61% vs 15%), diarrhea (57% vs 22%), fatigue/asthenia (57% vs

34%), hand-foot syndrome (50% vs 10%), hypertension (39% vs 14%), altered taste (38% vs 6%), nausea (34% vs 15%), dyspepsia (27% vs 7%), abdominal pain (25% vs 9%), hypothyroidism/TSH increased (24% vs 4%), rash (24% vs 12%), hair color changes (22% vs 2%). The most common grade 3/4 ARs reported in ≥5% of patients receiving SUTENT for adjuvant treatment of RCC and more commonly than in patients given placebo (vs placebo) were hand-foot syndrome (16% vs <1%), fatigue/asthenia (8% vs 2%), mucositis/stomatitis (6% vs 0%), and hypertension (8% vs 1%).

Most common grade 3/4 lab abnormalities (adjuvant RCC): The most common grade 3/4 lab abnormalities (occurring in ≥ 2% of patients receiving SUTENT) included neutropenia (13%), thrombocytopenia (5%), leukopenia (3%), lymphopenia (3%), elevated alanine aminotransferase (2%), elevated aspartate aminotransferase (2%), hyperglycemia (2%), and hyperkalemia (2%).

Most common ARs & most common grade 3/4 ARs (advanced RCC): The most common ARs reported in ≥20% of patients receiving SUTENT for treatment-naïve metastatic RCC (all grades, vs IFNα) 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 reported in ≥5% of patients with RCC receiving SUTENT (vs IFNα) 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 IFNα) 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%).

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

About Renal Cell Carcinoma (RCC)

Each year, approximately 304,000 new cases of kidney cancer are diagnosed worldwide, representing approximately 2-3 percent of all cancers.1,2,3 Renal cell carcinoma (RCC) is the most common type of kidney cancer, accounting for around 90 percent of cases.4 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.5 Patients at high risk of recurrence represent approximately 15 percent of all patients with primary resected RCC and approximately 60 percent of these patients will recur and develop metastatic disease within five years.6

About SUTENT® (sunitinib malate)

Sunitinib is a small molecule that inhibits multiple receptor tyrosine kinases, some of which are implicated in tumor growth, pathologic angiogenesis, and metastatic progression of cancer. Sunitinib was evaluated for its inhibitory activity against a variety of kinases (>80 kinases) and was identified as an inhibitor of platelet-derived growth factor receptors (PDGFRα and PDGFRβ), vascular endothelial growth factor receptors (VEGFR1, VEGFR2 and VEGFR3), stem cell factor receptor (KIT), Fms-like tyrosine kinase-3 (FLT3), colony stimulating factor receptor Type 1 (CSF-1R), and the glial cell-line derived neurotrophic factor receptor (RET).

Now approved in 119 countries across diagnoses, more than 350,000 patients worldwide have been treated with SUTENT.7 SUTENT is supported by an extensive body of evidence in scientific literature, including more than 440 publications.

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 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 health care products. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care 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 current as of November 16, 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 (sunitinib malate) and a new indication for SUTENT for the adjuvant treatment of adult patients at high risk of recurrent renal cell carcinoma following nephrectomy, 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, uncertainties regarding the commercial success of SUTENT in the new indication; the uncertainties inherent in research and development, 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 applications for SUTENT for the new indication may be filed in any other jurisdictions; whether and when any such other 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, 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 Ferlay J, Shin HR, Bray F.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(link is external). Accessed September 2016. 2 Ljungberg B, Campbell S and Choi H. The Epidemiology of Renal Cell Carcinoma. Eur Urol. 2011;60:615-621. 3 World Cancer Research Fund International: Kidney Cancer statistics. Available from: http://www.wcrf.org/int/cancer-facts-figures/data-specific-cancers/kidney-cancer-statistics. Accessed March 2016. 4 What is Kidney Cancer. James Whale Fund for Kidney Cancer. Available at: http://www.jameswhalefund.org/kidneycancer/what-is-kidney-cancer/(link is external). Accessed September 2016. 5 Based on comparison between 2015 Swedish population study (76%), Navigant interviews (95%), and Quant Pulse (79%). 2018-2022. 6 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. 7 Pfizer Data on File.

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