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U.S. Food And Drug Administration Approves Pfizer's INLYTA® (axitinib) For Patients With Previously Treated Advanced Renal Cell Carcinoma (RCC)

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First Treatment to Demonstrate Superior Benefit in a Phase 3 Study Compared with Another Targeted Agent in Advanced RCC

"The FDA approval of this new treatment represents a significant benefit for the many patients who are living with this type of kidney cancer and who are in need of additional treatment options,"

(BUSINESS WIRE)--Pfizer Inc. announced today that the U.S. Food and Drug Administration (FDA) has approved INLYTA® (axitinib), a kinase inhibitor, for the treatment of patients with advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy. The approval is based on data from the Phase 3 AXIS trial, which demonstrated that INLYTA significantly extended progression free survival (PFS) [HR=0.67, 0.54-0.81, P<0.0001] with a median PFS of 6.7 months (95% CI: 6.3, 8.6) compared with 4.7 months (95% CI: 4.6, 5.6) for those treated with sorafenib, a current standard of care for this patient population, representing a 43 percent improvement in median PFS compared to sorafenib.

Cancers of the kidney and renal pelvis are among the 10 most commonly diagnosed cancers in the United States[1]. Approximately 13,000 individuals die of advanced RCC in the U.S. each year[2]. Approximately 60,000 new cases of this tumor are diagnosed in the U.S. annually[1], about 20 percent of which have advanced disease at the time of diagnosis.[1] Between 40 and 65 percent of patients who progress following first-line therapy go on to receive a second-line treatment.[3,4,5]

"Even with the advent of targeted therapies, the need remains for additional options for patients with advanced RCC whose disease has progressed following first-line medications," said Dr. Mace Rothenberg, senior vice president of Clinical Development and Medical Affairs, Pfizer Oncology Business Unit. "INLYTA is the first targeted therapy to be approved in the U.S. for patients with advanced RCC after failure of one prior systemic therapy based on data demonstrating superior progression-free survival when compared to another FDA-approved, targeted agent."

"Pfizer has a strong commitment to advancing therapies for patients with advanced RCC," said Garry Nicholson, president and general manager, Pfizer Oncology Business Unit. "INLYTA is an important addition to our portfolio of treatment options for these patients, which also includes Sutent (sunitinib) and Torisel (temsirolimus)."

INLYTA, a kinase inhibitor, is an oral therapy that was designed to selectively inhibit vascular endothelial growth factor (VEGF) receptors 1, 2 and 3,which are receptors that can influence tumor growth, vascular angiogenesis and progression of cancer (the spread of tumors).[6,7]

“Through studying this drug we have learned that a VEGFR-targeted therapy can be effective following prior treatment options, including another VEGFR-targeted agent. This is important in helping physicians understand where these medications fit in the treatment armamentarium,” said Dr. Brian I. Rini, Taussig Cancer Institute at Cleveland Clinic, who served as principal investigator of this Pfizer-sponsored study and is a paid consultant to Pfizer Oncology.

"The FDA approval of this new treatment represents a significant benefit for the many patients who are living with this type of kidney cancer and who are in need of additional treatment options," said William Bro, chief executive officer of the Kidney Cancer Association.

Axitinib is also being investigated in a randomized clinical trial in patients with treatment-naïve as well as previously treated advanced RCC, and in a randomized Phase 2 clinical trial for the treatment of hepatocellular carcinoma (HCC).[8,9,10,11] Additionally, under a collaborative development agreement between Pfizer and SFJ Pharma Ltd. II, SFJ will conduct a Phase 3 clinical trial in Asia studying axitinib for adjuvant treatment of patients at high risk of recurrent RCC following nephrectomy. Healthcare professionals who are interested in learning more about Pfizer Oncology clinical trials that are open for enrollment can visit www.PfizerOncology.com/clinicaltrials. Patients with questions should contact their treating physician.

For more information and full prescribing information please visit www.InlytaHCP.com.

About Pfizer’s Patient Assistance Programs

Pfizer strongly believes patients should have access to medications they need, and has established reimbursement support services and patient assistance programs for them.

Pfizer is committed to helping eligible patients prescribed INLYTA gain access to the medication, and offers the Pfizer First Resource® Program to facilitate this process. The program can connect eligible insured patients to specialty pharmacies for reimbursement support services and to obtain their medicines. For uninsured and underinsured patients, the program can provide eligible patients with free medicine. We have also developed a co-pay assistance program for eligible privately-insured patients. Patients can call 1-877-744-5675 or visit www.INLYTAHCP.com to learn more.

INLYTA (axitinib) Indication and Important Safety Information

INLYTA is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

Hypertension including hypertensive crisis has been observed. Blood pressure should be well controlled prior to initiating INLYTA. Monitor for hypertension and treat as needed. For persistent hypertension, despite use of antihypertensive medications, reduce the dose.

Arterial and venous thrombotic events have been observed and can be fatal. Use with caution in patients who are at increased risk or who have a history of these events.

Hemorrhagic events, including fatal events, have been reported. INLYTA has not been studied in patients with evidence of untreated brain metastasis or recent active gastrointestinal bleeding and should not be used in those patients.

Gastrointestinal perforation and fistula, including death, have occurred. Use with caution in patients at risk for gastrointestinal perforation or fistula. Monitor for symptoms of gastrointestinal perforation or fistula periodically

throughout treatment.

Hypothyroidism requiring thyroid hormone replacement has been reported. Monitor thyroid function before initiation of, and periodically throughout, treatment.

Stop INLYTA at least 24 hours prior to scheduled surgery.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been observed. If signs or symptoms occur, permanently discontinue treatment.

Monitor for proteinuria before initiation of, and periodically throughout, treatment. For moderate to severe proteinuria, reduce the dose or temporarily interrupt treatment.

Liver enzyme elevation has been observed during treatment with INLYTA. Monitor ALT, AST, and bilirubin before initiation of, and periodically throughout, treatment.

For patients with moderate hepatic impairment, the starting dose should be decreased. INLYTA has not been studied in patients with severe hepatic impairment.

Women of childbearing potential should be advised of potential hazard to the fetus and to avoid becoming pregnant while receiving INLYTA.

Avoid strong CYP3A4/5 inhibitors. If unavoidable, reduce the dose. Avoid strong CYP3A4/5 inducers and, if possible, avoid moderate CYP3A4/5 inducers.

The most common (?20%) adverse events (AEs) occurring in patients receiving INLYTA (all grades) were diarrhea, hypertension, fatigue, decreased appetite, nausea, dysphonia, hand-foot syndrome, weight decreased, vomiting, asthenia and constipation.

The most common (?10%) grade 3/4 AEs occurring in patients receiving INLYTA were hypertension, diarrhea and fatigue.

The most common (?20%) lab abnormalities occurring in patients receiving INLYTA (all grades) included increased creatinine, decreased bicarbonate, hypocalcemia, decreased hemoglobin, decreased lymphocytes (absolute), increased ALP, hyperglycemia, increased lipase, increased amylase, increased ALT and increased AST.

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.

Important SUTENT(®) (sunitinib malate) Safety Information

Hepatotoxicity has been observed in clinical trials and postmarketing experience. This hepatotoxicity may be severe, and deaths have been reported. It is recommended to 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. SUTENT should not be restarted if patients subsequently experience severe changes in liver function tests or have other signs and symptoms of liver failure.

Women of child bearing age who are (or become) pregnant during therapy should be informed of the potential for fetal harm while on SUTENT.

Decreases in left ventricular ejection fraction (LVEF) to below the lower limit of normal (LLN) have been observed. Patients with concomitant cardiac conditions should be carefully monitored for clinical signs and symptoms of congestive heart failure. Patients should be monitored for hypertension and treated as needed with standard antihypertensive therapy. Complete blood counts (CBCs) with platelet count and serum chemistries should be performed at the beginning of each treatment cycle for patients receiving treatment with SUTENT.

The most common adverse reactions in gastrointestinal stromal tumor (GIST), RCC and pancreatic neuroendocrine tumor (NET) clinical trials were diarrhea, fatigue, asthenia, nausea, mucositis/stomatitis, anorexia, vomiting, neutropenia, hypertension, dyspepsia, abdominal pain, constipation, rash, hand-foot syndrome, skin discoloration, hair color changes, altered taste and bleeding.

For more information on SUTENT, including full prescribing information for SUTENT (sunitinib malate), please visit www.pfizer.com.

About Torisel® (temsirolimus)

Torisel is the only intravenous mammalian target of rapamycin (mTOR) inhibitor approved for the treatment of advanced renal cell carcinoma (RCC).

Based on preclinical studies, Torisel inhibits the activity of mTOR, an intracellular protein implicated in multiple growth-related cellular functions including proliferation, growth and survival. The inhibition of mTOR also reduces levels of certain growth factors, such as vascular endothelial growth factor (VEGF), which are overexpressed in solid tumors like kidney cancer and are thought to play a crucial role in angiogenesis, the process by which tumors acquire blood vessels, nutrients and oxygen needed for growth.

Important Torisel® (temsirolimus) Safety Information

TORISEL is contraindicated in patients with bilirubin >1.5 x ULN and should be used with caution when treating patients with mild hepatic impairment (bilirubin >1 – 1.5 x ULN or AST > ULN but bilirubin ? ULN). If TORISEL must be given to patients with mild hepatic impairment, reduce the dose of TORISEL to 15 mg/week. In a phase 1 study, the overall frequency of ? grade 3 adverse reactions and deaths, including deaths due to progressive disease, was greater in patients with baseline bilirubin > 1.5 x ULN.

Hypersensitivity/infusion reactions, including flushing, chest pain, dyspnea, hypotension, apnea, loss of consciousness, hypersensitivity and anaphylaxis, may occur very early in the first infusion or with subsequent infusions. Pretreat with an H1 antihistamine. TORISEL infusion should be interrupted in patients with infusion reactions and appropriate therapy given.

Serum glucose, serum cholesterol, and triglycerides should be tested before and during TORISEL treatment. TORISEL is likely to result in hyperglycemia and hyperlipemia. This may result in the need for an increase in the dose of, or initiation of, insulin and/or oral hypoglycemic agent therapy and/or lipid-lowering agents, respectively.

TORISEL may result in immunosuppression. Patients should be carefully observed for the occurrence of infections, including opportunistic infections.

Cases of interstitial lung disease, some resulting in death, have occurred. Some patients were asymptomatic or had minimal symptoms. Patients should undergo baseline radiography prior to TORISEL therapy and periodically thereafter, even in the absence of clinical respiratory symptoms. Follow patients closely and, if clinically significant respiratory symptoms develop, consider withholding TORISEL until recovery of symptoms and radiographic improvement of pneumonitis findings. Some patients required TORISEL discontinuation and/or treatment with corticosteroids and/or antibiotics.

Cases of fatal bowel perforation occurred with TORISEL. These patients presented with fever, abdominal pain, metabolic acidosis, bloody stools, diarrhea, and/or acute abdomen.

Cases of rapidly progressive and sometimes fatal acute renal failure not clearly related to disease progression occurred in patients who received TORISEL.

Due to abnormal wound healing, use TORISEL with caution in the perioperative period.

Patients with central nervous system tumors (primary CNS tumor or metastases) and/or receiving anticoagulation therapy may be at an increased risk of developing intracerebral bleeding (including fatal outcomes) while receiving TORISEL.

Live vaccinations and close contact with those who received live vaccines should be avoided.

TORISEL may cause fetal harm. Patients and their partners should be advised to avoid pregnancy throughout treatment and for 3 months after TORISEL therapy has stopped.

Elderly patients may be more likely to experience certain adverse reactions including diarrhea, edema and pneumonia.

The most common (incidence ?30%) adverse reactions observed with TORISEL are: rash (47%), asthenia (51%), mucositis (41%), nausea (37%), edema (35%), and anorexia (32%). The most common laboratory abnormalities (incidence ?30%) are anemia (94%), hyperglycemia (89%), hyperlipemia (87%), hypertriglyceridemia (83%), elevated alkaline phosphatase (68%), elevated serum creatinine (57%), lymphopenia (53%), hypophosphatemia (49%), thrombocytopenia (40%), elevated AST (38%), and leukopenia (32%).

Most common grades 3/4 adverse events and laboratory abnormalities included asthenia (11%), dyspnea (9%), hemoglobin decreased (20%), lymphocytes decreased (16%), glucose increased (16%), phosphorus decreased (18%), and triglycerides increased (44%).

Pleural effusion, hemodynamically significant pericardial effusions requiring intervention, convulsions, rhabdomyolysis, Stevens-Johnson Syndrome, complex regional pain syndrome and extravasations have been reported during postmarketing use.

Strong inducers of CYP3A4/5 (eg, dexamethasone, rifampin) and strong inhibitors of CYP3A4 (eg, ketoconazole, atazanavir) may decrease and increase concentrations of the major metabolite of TORISEL, respectively. If alternatives cannot be used, dose modifications of TORISEL are recommended.

Avoid St. John’s Wort which may decrease TORISEL plasma concentrations, and grapefruit juice which may increase plasma concentrations of the major metabolite of TORISEL.

The combination of TORISEL and sunitinib resulted in dose-limiting toxicity (Grade 3/4 erythematous maculopapular rash, and gout/cellulitis requiring hospitalization).

For more information on TORISEL, including full prescribing information for TORISEL (temsirolimus), please visit www.pfizer.com.

About Pfizer Oncology

Pfizer Oncology is committed to the discovery, investigation and development of innovative treatment options to improve the outlook for cancer patients worldwide.

As a leader in the treatment of advanced RCC, Pfizer Oncology is dedicated to offering multiple treatments and investigating new agents in different populations and stages of disease.

For more information please visit www.Pfizer.com.

DISCLOSURE NOTICE: The information contained in this release is as of January 27, 2012. The Company assumes no obligation to update forward-looking statements contained in this release as a result of new information or future events or developments.

This release contains forward-looking information about certain potential additional indications for axitinib, including their potential benefits, that involves substantial risks and uncertainties. Such risks and uncertainties include, among other things, the uncertainties inherent in research and development; decisions by regulatory authorities regarding whether and when to approve any drug applications that may be filed for such additional indications, as well as their decisions regarding labeling and other matters that could affect their availability or commercial potential; 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, 2010 and in its reports on Form 10-Q and Form 8-K.

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