Pfizer Provides Update on Phase 3 Trial of Axitinib as Adjuvant Treatment for Patients at High Risk of Renal Cell Carcinoma Recurrence After Surgery

Tuesday, April 10, 2018 - 10:00am

Pfizer Inc. today announced that the independent Data Monitoring Committee for the Phase 3 ATLAS trial evaluating INLYTA® (axitinib) as adjuvant therapy for patients at high risk of recurrent renal cell carcinoma (RCC) after nephrectomy recommended stopping the trial at a planned interim analysis due to futility. The recommendation was based on the study failing to demonstrate a clear improvement in the primary endpoint of extending disease-free survival (DFS) for patients treated with INLYTA compared with patients treated with placebo. No new safety signals were observed, and the safety profile was consistent with the known profile of INLYTA in advanced RCC.

“We are disappointed by the outcome of this study as we had hoped the efficacy that INLYTA has demonstrated as a second-line treatment in patients with advanced renal cell carcinoma would carry over to patients with earlier stage disease, where it would delay or prevent disease relapse. That goal was not achieved. We will conduct additional analyses on the data that may provide insight into this result. Studies evaluating INLYTA in combination with immune checkpoint inhibitors for patients with a variety of advanced stage cancers, including RCC, will continue,” said Mace Rothenberg, M.D., Chief Development Officer, Oncology, Pfizer Global Product Development.

Detailed efficacy and safety data from ATLAS will be submitted for presentation at a future medical meeting.

INLYTA has had a significant impact on the treatment of patients with advanced RCC worldwide in its currently approved indications, supported by an extensive body of evidence in scientific literature including more than 50 publications. More than 66,000 patients have been treated with INLYTA to date.1 For more information on INLYTA, please visit www.INLYTA.com.

About RCC

Each year, approximately 338,000 new cases of kidney cancer are diagnosed worldwide, representing approximately 2-3 percent of all cancers.2,3,4 Renal cell carcinoma (RCC) is the most common type of kidney cancer, accounting for around 90 percent of cases.5 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.6 However, a subset will relapse after surgery and once their disease becomes metastatic, their long-term prognosis is poor in advanced RCC with a 5-year survival rate as low as 12%.7

About ATLAS

ATLAS (A Randomized Double-Blind Phase 3 Study of Adjuvant Axitinib Versus Placebo in Subjects at High Risk of Recurrent RCC)(NCT01599754) is a global, multicenter, randomized double-blind Phase 3 trial that investigated the clinical efficacy and safety of adjuvant INLYTA (5 mg twice daily) versus placebo in patients (n=724) at high risk of recurrent RCC following nephrectomy. Patients were dosed up to 3 years (for a minimum of 1 year) in the study and the primary endpoint was disease-free survival (DFS). The study was conducted in collaboration with SFJ Pharmaceuticals, who provided the funding and clinical development supervision to generate the clinical data.

About INLYTA® (axitinib)

INLYTA is an oral therapy that is designed to inhibit tyrosine kinases, including vascular endothelial growth factor (VEGF) receptors 1, 2 and 3; these receptors can influence tumor growth, vascular angiogenesis and progression of cancer (the spread of tumors). In the U.S., INLYTA is approved for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy. INLYTA is also approved by the European Medicines Agency (EMA) for use in the EU in adult patients with advanced RCC after failure of prior treatment with sunitinib or a cytokine.

INLYTA Important Safety Information

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. Discontinue INLYTA if hypertension is severe and persistent despite use of antihypertensive therapy and dose reduction of INLYTA, and discontinuation should be considered if there is evidence of hypertensive crisis.

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. If any bleeding requires medical intervention, temporarily interrupt the INLYTA dose.

Cardiac failure has been observed and can be fatal. Monitor for signs or symptoms of cardiac failure throughout treatment with INLYTA. Management of cardiac failure may require permanent discontinuation of INLYTA.

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.

No formal studies of the effect of INLYTA on wound healing have been conducted. 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. Grapefruit or grapefruit juice may also increase INLYTA plasma concentrations and should be avoided.

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, vs sorafenib) were diarrhea (55% vs 53%), hypertension (40% vs 29%), fatigue (39% vs 32%), decreased appetite (34% vs 29%), nausea (32% vs 22%), dysphonia (31% vs 14%), hand-foot syndrome (27% vs 51%), weight decreased (25% vs 21%), vomiting (24% vs 17%), asthenia (21% vs 14%), and constipation (20% vs 20%).

The most common (≥10%) grade 3/4 AEs occurring in patients receiving INLYTA (vs sorafenib) were hypertension (16% vs 11%), diarrhea (11% vs 7%), and fatigue (11% vs 5%).

The most common (≥20%) lab abnormalities occurring in patients receiving INLYTA (all grades, vs sorafenib) included increased creatinine (55% vs 41%), decreased bicarbonate (44% vs 43%), hypocalcemia (39% vs 59%), decreased hemoglobin (35% vs 52%), decreased lymphocytes (absolute) (33% vs 36%), increased ALP (30% vs 34%), hyperglycemia (28% vs 23%), increased lipase (27% vs 46%), increased amylase (25% vs 33%), increased ALT (22% vs 22%), and increased AST (20% vs 25%).

For more information and full Prescribing Information, visit www.INLYTA.com.

About the SFJ Pharmaceuticals Group

SFJ is a global drug development company, which provides a unique and highly customized co-development partnering model for the world's top pharmaceutical and biotechnology companies. SFJ provides at-risk funding and the global clinical development management and oversight, necessary for regulatory submission for some of the most promising drug development programs of Pharmaceutical and Biotechnology companies. SFJ’s mission is to leverage its financial strength and global team of pharmaceutical development experts to accelerate the development of life-saving and life enhancing drugs for the benefit of physicians and the patients they serve.

About Pfizer Oncology

Pfizer Oncology is committed to pursuing innovative treatments that have a meaningful impact on people living with cancer. Our growing pipeline of biologics, small molecules, and immunotherapies is focused on identifying and translating the best scientific breakthroughs into clinical application for patients across a diverse array of solid tumors and hematologic cancers. Today, we have 10 approved oncology medicines and 17 assets currently in clinical development. By maximizing our internal scientific resources and collaborating with other companies, government and academic institutions, as well as non-profit and professional organizations, we are bringing together the brightest and most enterprising minds to take on the toughest cancers. Together we can accelerate breakthrough treatments to patients around the world and work to redefine life with cancer.

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 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 as of April 10, 2018. 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 INLYTA (axitinib), including its 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 impact of the Phase 3 ATLAS trial results; the uncertainties inherent in research and development, including the ability to meet anticipated clinical trial

completion dates and 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; the risk that clinical trial data are subject to differing interpretations; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when any drug applications may be filed for INLYTA in combination with immune checkpoint inhibitors in any jurisdictions; whether and when regulatory authorities may approve any such applications, which will depend on the assessment by such regulatory authority of the benefit-risk profile suggested by the totality of the efficacy and safety information submitted and, if approved, whether INLYTA will be commercially successful; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of INLYTA; 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, 2017 and its subsequent reports of 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.

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1 Pfizer data on file. 2 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 April 2018. 3 Ljungberg B, Campbell S and Choi H. The Epidemiology of Renal Cell Carcinoma. Eur Urol. 2011;60:615-621. 4 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 April 2018. 5 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 April 2018. 6 Based on comparison between 2015 Swedish population study (76%), Navigant interviews (95%), and Quant Pulse (79%). 2018-2022. 7 The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI). Cancer Stat Facts: Kidney and Renal Pelvis Cancer. https://seer.cancer.gov/statfacts/html/kidrp.html. Accessed April 2018.

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