Merck Receives Priority Review From FDA for New Drug Application for HIF-2α Inhibitor Belzutifan (MK-6482)

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Application Based on Objective Response Rate From Phase 2 Trial Evaluating Belzutifan in Patients With Von Hippel-Lindau Disease-Associated Renal Cell Carcinoma

New Filing Further Strengthens Merck’s Expanding and Diverse Oncology Portfolio

KENILWORTH, N.J.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that the U.S. Food and Drug Administration (FDA) has accepted and granted priority review for a New Drug Application (NDA) for the hypoxia-inducible factor-2 alpha (HIF-2α) inhibitor belzutifan (pronounced bell-ZOO-ti-fan), a novel investigational candidate in Merck’s oncology pipeline, for the potential treatment of patients with von Hippel-Lindau (VHL) disease-associated renal cell carcinoma (RCC), not requiring immediate surgery. This NDA is based on data from the Phase 2 Study-004 trial, in which belzutifan showed a confirmed overall response rate of 36.1% (n=22/61) (95% CI: 24.2-49.4) in patients with VHL disease-associated RCC. The FDA has set a Prescription Drug User Fee Act (PDUFA), or target action, date of September 15, 2021.

“Von Hippel-Lindau disease is a rare genetic condition for which there is no systemic treatment option available and is associated with a high risk of cancer development in multiple organs. In fact, up to 70% of patients with VHL develop renal cell carcinoma during their lifetime,” said Dr. Scot Ebbinghaus, vice president, clinical research, Merck Research Laboratories. “This priority review validates the important progress we have made to expand and diversify Merck’s oncology pipeline with innovative, new therapeutic approaches. We look forward to working closely with the FDA to bring belzutifan to patients in need.”
Merck is also studying belzutifan in advanced RCC and other tumor types through a broad clinical program. In addition to the ongoing Phase 2 Study-004 trial, belzutifan is being evaluated in Phase 3 trials as monotherapy and as part of a combination regimen in previously treated patients and as part of a combination regimen as a first-line treatment for advanced clear cell RCC.

About the Phase 2 Study-004 Trial

This application is based on data from Study-004 (ClinicalTrials.gov, NCT03401788), which is a Phase 2, open-label trial evaluating belzutifan for the potential treatment of patients with VHL disease who had at least one measurable solid tumor localized to the kidney and who did not require immediate surgery. The study enrolled 61 patients who received belzutifan 120 mg orally once daily until disease progression or unacceptable toxicity. The primary endpoint was objective response rate in VHL disease-associated RCC. Secondary endpoints in RCC tumors include disease control rate, duration of response, time to response, progression-free survival, time to surgery and safety.

Additionally, this study evaluated response rates in other common VHL disease-associated tumors, including pancreatic cysts, pancreatic neuroendocrine tumors, central nervous system (CNS) hemangioblastomas, and retinal hemangioblastomas.

About Belzutifan

Belzutifan (MK-6482) is a novel, potent and selective inhibitor of HIF-2α. Proteins known as hypoxia-inducible factors, including HIF-2α, can accumulate in patients when VHL, a tumor-suppressor protein, is inactivated. If not properly regulated, the accumulation of HIF-2α can stimulate several oncogenes associated with cellular proliferation, angiogenesis and tumor growth, leading to the growth of both benign and malignant tumors. This inactivation of VHL has been observed in more than 90% of clear cell RCC tumors. Research into VHL biology that led to the discovery of HIF-2α was awarded the Nobel Prize in Physiology or Medicine in 2019.

About Von Hippel-Lindau Disease and Renal Cell Carcinoma

Von Hippel-Lindau disease is a rare genetic disease that affects one in 36,000 people (200,000 cases worldwide and 10,000 cases in the U.S. alone). Patients with VHL disease are at risk for benign blood vessel tumors as well as several cancers, including RCC. As many as 70% of people with VHL disease develop RCC.

Renal cell carcinoma is by far the most common type of kidney cancer; about nine of 10 kidney cancers are RCCs, and about seven of 10 RCCs are clear cell. Worldwide, it is estimated there were nearly 431,300 cases of kidney cancer diagnosed and almost 179,400 deaths from the disease in 2020. In the U.S. alone, it is estimated there will
be almost 76,100 new cases of kidney cancer diagnosed and nearly 13,800 deaths from the disease in 2021.

Merck's Focus on Cancer

Our goal is to translate breakthrough science into innovative oncology medicines to help people with cancer worldwide. At Merck, the potential to bring new hope to people with cancer drives our purpose and supporting accessibility to our cancer medicines is our commitment. As part of our focus on cancer, Merck is committed to exploring the potential of immuno-oncology with one of the largest development programs in the industry across more than 30 tumor types. We also continue to strengthen our portfolio through strategic acquisitions and are prioritizing the development of several promising oncology candidates with the potential to improve the treatment of advanced cancers. For more information about our oncology clinical trials, visit www.merck.com/clinicaltrials.

About Merck

For 130 years, Merck, known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world’s most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit www.merck.com and connect with us on Twitter, Facebook, Instagram, YouTube and LinkedIn.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment;
technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2020 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site (www.sec.gov).

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