Pfizer Presents Positive Data from Phase 2 Study of Ponsegromab in Patients with Cancer Cachexia

Saturday, September 14, 2024 - 08:45am

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Study met primary endpoint of change from baseline in body weight for ponsegromab compared to placebo across all ponsegromab doses tested, reaching 5.6% mean increase at the highest dose evaluated at 12 weeks; ponsegromab was generally considered safe and well-tolerated at all dose levels i At the highest dose evaluated, improvements were seen from baseline in appetite and cachexia symptoms, physical activity, and muscle mass i Based on positive Phase 2 results, registration-enabling studies will start in 2025

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced its Phase 2 study of ponsegromab, a monoclonal antibody directed against growth differentiation factor-15 (GDF-15), met its primary endpoint of change from baseline in body weight compared to placebo in people with cancer cachexia and elevated levels of GDF-15. Cachexia is a common, life-threatening wasting condition that can significantly impact quality of life in affected patients with cancer. ii,iii Results will be presented today as a late-breaking Proffered Paper Presentation (LBA82) at the European Society for Medical Oncology (ESMO) 2024 Congress and have simultaneously been published in The New England Journal of Medicine (NEJM) .

“Cachexia is a common condition in cancer patients, associated with weight loss, functional decline, and ultimately poor outcomes. Despite the number of people suffering from cachexia, there are no available options for us to help treat patients,” said Jeffrey Crawford, M.D., George Barth Geller Professor for Research at Duke Cancer Institute, and principal investigator. “This study showed us those who received ponsegromab had

improvement in body weight, muscle mass, quality of life, and physical function. These findings offer hope that a breakthrough targeted treatment is potentially on the horizon for our patients.”

The Phase 2 study included 187 participants with non-small cell lung cancer, pancreatic cancer, or colorectal cancer. Ponsegromab demonstrated significant and robust increases in body weight after 12 weeks across all doses: 2.02% (95% confidence interval (CI), -0.97 to 5.01%) in the 100 mg treatment group, 3.48% (95% CI, 0.54 to 6.42%) in the 200 mg group, and 5.61% (95% CI, 2.56 to 8.67%) in the 400 mg group, compared to placebo. Improvements across multiple domains of the cachexia phenotype were observed in the 400 mg group including in measures of appetite and cachexia symptoms, physical activity and skeletal muscle index. No clinically significant adverse trends were noted with ponsegromab administration. Treatment related adverse events occurred in 8.9% of patients taking placebo and 7.7% of patients taking ponsegromab. i

“Discovered and developed in-house at Pfizer, ponsegromab represents our ability to translate deep scientific expertise into patient benefit,” said Charlotte Allerton, Head of Discovery and Early Development, Pfizer. “These results provide strong evidence that we have unlocked a mechanism to interrupt a critical driver of cachexia, GDF-15, which has the potential to impact patients with cancer cachexia and other life-threatening conditions. We look forward to advancing this program as part of our broader cardiometabolic portfolio to address weight management across the spectrum of patient need.”

Based on these positive results, Pfizer is discussing late-stage development plans with regulators with the goal of starting registration-enabling studies in 2025. Ponsegromab is also being investigated in a Phase 2 study in patients with heart failure (HF) and elevated serum GDF-15 concentrations (NCT05492500).

About the Phase 2 Trial in Cancer Cachexia The primary objective of the Phase 2 study (NCT05546476) is to assess the effect of ponsegromab on body weight in patients with cancer (non-small cell lung cancer, pancreatic cancer or colorectal cancer), cachexia and elevated serum GDF-15 concentrations (> 1500 pg/mL). Secondary and exploratory endpoints objectives included measures such as: Change from baseline in appetite and cachexia symptoms, digital measures of physical activity, and changes in lumbar skeletal muscle index (LSMI). Patients (n=187) received either ponsegromab (100 mg, 200 mg or 400 mg) or placebo once every four weeks subcutaneously for 12 weeks.

About Cachexia Cachexia is a complex, disabling, and life-threatening metabolic condition that is estimated to affect about 9 million people worldwide. ii Symptoms such as weight

and muscle loss can reduce patients' ability to tolerate treatment for their underlying chronic diseases, such as cancer and heart failure, and can severely impact quality of life. ii , iii In cancer, cachexia can diminish the efficacy of cancer treatments and is thought to contribute to decreased survival rates and may cause up to 30% of cancer-related deaths. iv Despite its severity, there are no FDA-approved treatments for cachexia. iii

About Ponsegromab Ponsegromab is an investigational monoclonal antibody designed to treat cachexia by targeting GDF-15. Prior Phase 1b data in participants with cancer cachexia demonstrated proof-of-mechanism for ponsegromab with robust suppression of unbound circulating GDF15 levels observed . The results showed encouraging signals of efficacy that included increases in body weight and encouraging improvements in patient reported outcomes.

About Pfizer: Breakthroughs That Change Patients' Lives 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, including innovative medicines and vaccines. 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 175 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 X 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 14, 2024. 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 ponsegromab, an investigational monoclonal antibody designed to treat cachexia, including its potential benefits and late-stage development planning, and Pfizer's cardiometabolic portfolio, that involve 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 clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch

dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data, including results from the Phase 2 study of ponsegromab in patients with heart failure; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any jurisdictions for any potential indication for ponsegromab or any other cardiometabolic product candidates; whether and when any such applications that may be filed for ponsegromab or any other such product candidates may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether ponsegromab or any such other product candidates will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of ponsegromab or any such other product candidates; uncertainties regarding the impact of COVID-19 on our business, operations and financial results; 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, 2023, 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 .

_____ i Groarke J, et al. Ponsegromab for the Treatment of Cancer Cachexia. The New England Journal of Medicine . https://doi.org/10.1056/NEJMoa2409515 . Accessed September 14, 2024. ii Cleveland Clinic. Cachexia (Wasting Syndrome). Cachexia (Wasting Syndrome): Symptoms & Treatment (clevelandclinic.org) . Accessed September 3, 2024. iii Lisa Martin, Michael B. Sawyer, Cancer Cachexia: Emerging Preclinical Evidence and the Pathway Forward to Clinical Trials, JNCI: Journal of the National Cancer Institute , Volume 107, Issue 12, December 2015, https://doi.org/10.1093/jnci/djv322 iv National Cancer Institute. Cancer Cachexia: After Years of No Advances, Progress Looks Possible. Treating Cancer Cachexia: Progress Looks Possible - NCI . Accessed September 3, 2024.

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