Pfizer Announces Positive Results from Fifth Phase 3 Trial of Abrocitinib, Evaluating Safety and Efficacy Across Different Dosing Regimens

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-Following an initial 12-week induction treatment phase, fewer patients treated with abrocitinib experienced a flare than those on placebo at any point in the trial over 40 weeks-

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) announced today positive top-line results from the Phase 3 JADE REGIMEN study. This 52-week study investigated abrocitinib, an investigational oral once-daily Janus kinase 1 (JAK1) inhibitor, in patients 12 and older with moderate to severe atopic dermatitis (AD) following response to initial open label induction treatment with abrocitinib 200mg. Patients were randomized into one of three arms: 200mg, 100mg, or placebo. Both doses of abrocitinib met the primary endpoint, resulting in significantly fewer patients experiencing a loss of response requiring rescue treatment, or “flaring,” compared to those randomized to placebo. Both doses also met the key secondary endpoint of a larger percentage of patients maintaining an Investigator’s Global Assessment (IGA) response of clear or almost clear relative to placebo.

“Atopic dermatitis brings a lot of uncertainty and disruption to daily life, and the unpredictability of flares can make treating and managing the disease complex and frustrating,” said Michael Corbo, PhD, Chief Development Officer, Inflammation & Immunology, Pfizer Global Product Development. “These latest results from our Phase 3 clinical trial program shed light on the potential abrocitinib, if approved, could have to

prevent troublesome flares in patients.”

JADE REGIMEN Top-Line Results

The study met its primary and key secondary endpoints. After achieving clinical response in the induction period, patients who continued on the higher dose of abrocitinib, 200mg, or switched to the lower dose, 100mg, had a significantly higher probability of not experiencing a flare compared to those on placebo through week 52 (81.1%, 57.4%, and 19.1%, respectively; $p<0.0001$ for both doses versus placebo). In addition, patients who continued on the higher dose of abrocitinib were significantly less likely to flare than those on the lower dose ($p<0.0001$). Patients on either dose of abrocitinib were significantly more likely to maintain an IGA score of clear (zero) or almost clear (one) compared to placebo ($p<0.0001$ for both doses versus placebo).

The primary endpoint after treatment in the 12-week induction phase was the loss of response requiring rescue treatment among groups during the blinded treatment period up to 40 weeks. Loss of response requiring rescue treatment, or a “flare,” was defined as a loss of at least 50% of the Eczema Area and Severity Index (EASI) response at week 12 and an IGA score of two or higher (on a five-point scale). The key secondary endpoint was the loss of response based on an IGA score of two or higher.

Out of 1,233 subjects enrolled, 798 (64.7%) responded during the initial 12-week induction period with abrocitinib monotherapy (200mg, once daily), a higher than expected responder rate compared to the monotherapy studies JADE MONO-1 and JADE MONO-2. Responder criteria was defined as achieving an IGA score of clear (zero) or almost clear (one), a reduction from IGA baseline of at least two points, and reaching an EASI-75 response compared to baseline.

No new safety signals were observed in the trial. Safety results showed that during the induction period 66.5% of patients experienced an adverse event and 1.6% experienced a serious adverse event. Following randomization, a higher percentage of patients receiving either the 200mg or 100mg dose of abrocitinib experienced adverse events compared to placebo (63.2%, 54%, and 45.3%, respectively). The percentage of patients who experienced serious adverse events were 4.9%, 1.5%, and 0.7%, respectively. More patients treated with abrocitinib discontinued from the study due to adverse events (6%, 1.9%, and 1.5%, respectively). One patient died from gastric adenocarcinoma 208 days following discontinuation from the induction treatment period, which was deemed unrelated to the study drug by the investigator.

Additional Details About the JADE REGIMEN Study

JADE REGIMEN was a 52-week, randomized, responder-enriched, double-blind, placebo-controlled, Phase 3 withdrawal trial enrolling 1,233 subjects globally. The trial included a 12-week open-label run-in period to determine responder status to an initial induction treatment with abrocitinib monotherapy (200mg, once daily). Patients in the open-label run-in period did not receive any topical therapy. Subjects with a positive clinical response to abrocitinib induction treatment at the end of the 12-week open-label run-in period entered a 40-week, double-blind, maintenance treatment period in which they were randomized into one of three treatment arms in a 1:1:1 ratio: placebo, abrocitinib 100mg once daily, or abrocitinib 200mg once daily. Medicated topical and/or systemic standard of care therapies were not allowed during the open-label run-in and blinded treatment periods.

During the blinded treatment period, subjects meeting the protocol definition of flare entered an open-label rescue period during which they receive another 12-week course of abrocitinib 200mg once daily with topical therapy per local standard of care (SOC). In this study, flare requiring rescue treatment was defined as a loss of at least 50% of the EASI response at week 12 and an IGA score of two or higher.

Eligible subjects completing the 40 weeks of blinded treatment, or a full 12-week rescue treatment period, had the option to enter a long-term extension (LTE) study, B7451015. Subjects discontinuing early from treatment, or who were otherwise ineligible for the LTE study, entered a four-week follow up period in this study.

JADE REGIMEN is the fifth trial in the JAK1 Atopic Dermatitis Efficacy and Safety (JADE) global development program. Pfizer announced complete results from the second trial in the program, JADE MONO-2, as well as top-line results from the JADE TEEN and JADE COMPARE studies, earlier this year. Additionally, complete results from JADE MONO-1 were published in The Lancetin July 2020. Additional data from other studies in the JADE program will be available in the coming months.

Full results from JADE REGIMEN will be submitted for presentation at a future scientific meeting and publication in a medical journal.

For additional information about JADE REGIMEN, please visit https://www.clinicaltrials.gov.

About Abrocitinib

Abrocitinib is an oral small molecule that selectively inhibits Janus kinase (JAK) 1. Inhibition of JAK1 is thought to modulate multiple cytokines involved in pathophysiology of atopic dermatitis, including interleukin (IL)-4, IL-13, IL-31, IL-22, and thymic stromal

lymphopoietin (TSLP).

In October 2020, Pfizer announced that the U.S. Food and Drug Administration (FDA) granted Priority Review designation to the company's New Drug Application (NDA) for abrocitinib 100mg and 200mg for the treatment of moderate to severe AD in patients 12 and older, with a decision expected in April 2021. Priority Review designation is granted to medicines that the FDA considers to have the potential to provide significant improvements in the safety and effectiveness of the treatment, prevention or diagnosis of a serious condition. Abrocitinib received Breakthrough Therapy designation from the FDA for the treatment of patients with moderate to severe AD in February 2018.

The European Medicines Agency (EMA) has also accepted the Marketing Authorization Application (MAA) for abrocitinib in the same patient population with a decision anticipated in the second half of 2021.

Abrocitinib also received a Promising Innovative Medicine (PIM) designation from the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) earlier this year, which indicates that a product may be eligible for the early access to medicines scheme (EAMS) based on early clinical data. EAMS aims to give patients with life threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization when there is a clear unmet medical need.

About Atopic Dermatitis

AD is a chronic skin disease characterized by inflammation of the skin and skin barrier defects.1,2 Lesions of AD are characterized by erythema (skin turning red or purple depending on normal skin color), itching, induration (hardening)/papulation (formulation of papules), and oozing/crusting.2,3

AD is one of the most common, chronic, relapsing childhood dermatoses, affecting up to 10% of adults and up to 20% of children worldwide.3,4

About Pfizer's Immunokinase Inhibitor Leadership

The JAK pathways are believed to play an important role in inflammatory processes as they are involved in signaling for over 50 cytokines and growth factors, many of which drive immune-mediated conditions.5 JAK inhibition may offer patients with these conditions a potential new advanced treatment option.6

Pfizer's leading JAK biology and chemistry expertise, combined with our research experience, has uniquely enabled the company to take a different R&D approach to that

of other companies involved in JAK research, resulting in one of the broadest immunokinase inhibitor pipelines. Instead of studying a single molecule for all its potential uses, where it may not be optimal for some, Pfizer’s candidates with unique selectivity profiles are purposefully matched to the conditions where we believe they have the greatest potential to, if approved, address unmet need. Pfizer has five unique immunokinase inhibitors in late-stage clinical trials for the potential treatment of ten immune-mediated diseases:

Abrocitinib: A JAK1 inhibitor currently under regulatory review by the FDA and EMA for the potential treatment of moderate-to-severe AD among adolescents and adults Ritlecitinib (PF-06651600): An oral, JAK3/TEC family kinase inhibitor in a phase 3 clinical trial for the potential treatment of alopecia areata (AA) and in phase 2 for vitiligo, Crohn’s disease (CD), and ulcerative colitis (UC) Brepocitinib (PF-06700841): A tyrosine kinase 2(TYK2)/JAK1 inhibitor in phase 2 clinical trials for the potential treatment of psoriasis and AD in topical formulation, and, in oral formulation for psoriatic arthritis, CD, UC, vitiligo, systemic lupus erythematosus (SLE), AA and hidradenitis suppurativa (HS) PF-06826647: A TYK2 inhibitor under investigation in phase 2 clinical trials for the potential treatment of psoriasis and HS PF-06650833: An IL-1 receptor associated kinase 4 (IRAK4) inhibitor under investigation for the potential treatment of rheumatoid arthritis and HS in phase 2 clinical trials
Pfizer Inc.: 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 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 November 11, 2020. 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 a product candidate, abrocitinib, regulatory filings with the FDA and EMA for abrocitinib, and Pfizer's ongoing investigational programs in kinase inhibitor therapies, 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, 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; 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 other jurisdictions for any potential indication for abrocitinib or in any jurisdictions for any other investigational kinase inhibitor therapies; whether and when the applications for abrocitinib pending with the FDA and EMA may be approved and whether and when any such other applications 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 abrocitinib or any such other investigational kinase inhibitor therapies 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 abrocitinib or any other investigational kinase inhibitor therapies; 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, 2019 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.

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Ann Nutr Metab. 2015;66(suppl 1):8-16. 5 Banerjee, S., Biehl, A., Gadina, M. et al. JAK–STAT Signaling as a Target for Inflammatory and Autoimmune Diseases: Current and Future Prospects. Drugs. 2017;77: 521. https://doi.org/10.1007/s40265-017-0701-9. 6 Telliez JB, Dowty ME, Wang L, Jussif J, Lin T, Li L, et al. Discovery of a JAK3-selective inhibitor: functional differentiation of JAK3-selective inhibition over pan-JAK or JAK1-selective inhibition. ACS Chem Biol. 2016;11(12):3442–51. doi:10.1021/acschembio.6b00677.

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