

Early amcenenstrant data featured at ASCO support its potential to become a new endocrine backbone therapy for ER+/HER2- breast cancer

- * Amcenenstrant, an investigational oral selective estrogen receptor degrader (SERD), achieved an objective response rate of 34% and a clinical benefit rate of 74% in Phase 1 study (AMEERA-1) in combination with palbociclib
- * Overall safety profile of amcenenstrant with palbociclib is consistent with what was observed in monotherapy, without signs of significant cardiac or ocular side effects
- * The Phase 3 combination study (AMEERA-5) of amcenenstrant with palbociclib in the first-line setting was initiated in October 2020 and is successfully recruiting patients
- * The pivotal study (AMEERA-3) of amcenenstrant versus physician's choice in locally advanced or metastatic estrogen receptor-positive (ER+) breast cancer is fully recruited; readout expected in H2 2021

PARIS – May 19, 2021 – Phase 1 data from the AMEERA-1 study evaluating amcenenstrant, an investigational oral selective estrogen receptor degrader (SERD), will be presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting. In a pooled analysis, amcenenstrant in combination with palbociclib showed encouraging antitumor activity in postmenopausal women with estrogen receptor-positive (ER+)/human epidermal growth factor receptor 2-negative (HER2-) metastatic breast cancer (MBC).

“These early clinical data show that the combination of amcenenstrant with palbociclib achieved encouraging antitumor activity,” said Sarat Chandarlapaty, M.D., Ph.D., Medical Oncologist, Memorial Sloan Kettering Cancer Center. “The analysis also demonstrated no clinically significant cardiac or ocular findings and an overall safety profile in line with what we saw in the monotherapy setting. It’s notable to see this kind of activity in patients with ER+ metastatic breast cancer, where there is a clear need for new therapeutic options.”

In this preliminary analysis from the open-label AMEERA-1 study, amcenenstrant was evaluated in dose escalation cohorts (Part C) at 200mg (n=9) and 400mg (n=6) daily and in a dose expansion cohort (Part D; n=30) at 200mg daily, all in combination with a standard dose of palbociclib. Eligible patients included post-menopausal women with ER+/HER2- MBC who were pre-treated with endocrine therapy in the advanced setting for at least six months or had resistance to adjuvant endocrine therapy.

In the pooled population exposed with amcenestrant at 200mg daily evaluable for response (n=35), the objective response rate (ORR) was 34% (90% CI: 21.1-49.6), with confirmed partial responses (PR) in 12/35 patients, and the clinical benefit rate (CBR) was 74% (90% CI: 59.4-85.9), with clinical benefit in 26/35 patients at 24 weeks. Amcenestrant 200mg daily in combination with palbociclib demonstrated a favorable overall safety profile (n=39), with treatment related adverse events (TRAEs) attributable to amcenestrant similar to those observed with monotherapy. For all grade events, amcenestrant TRAEs occurred in 72% and to palbociclib in 90% of patients, and for grade ≥ 3 in 15% and 46% of patients, respectively. The most frequent non-hematological amcenestrant TRAEs included fatigue (18%) and nausea (18%), all grade ≤ 2 . No clinically significant cardiac or ocular safety findings occurred.

“The Phase 3 AMEERA-5 study was built upon promising preclinical and clinical data, including the data presented here at ASCO, and expands our knowledge of amcenestrant as a potential best-in-class oral endocrine backbone therapy for ER+/HER2- breast cancer,” said John Reed, M.D., Ph.D., Global Head of Research and Development at Sanofi. “A significant need exists for more treatment options for ER+ breast cancer, the most common type of breast cancer, accounting for approximately 75% of all breast cancers diagnosed today.”

Amcenestrant is an oral SERD that antagonizes and degrades the estrogen receptor (ER) resulting in inhibition of the ER signaling pathway. Amcenestrant is currently under clinical investigation and its safety and efficacy have not been evaluated by any regulatory authority.

Amcenestrant clinical development program

The comprehensive development program for amcenestrant has been designed to evaluate its role: (1) as a single agent in second-line or later lines of treatment of ER+/HER2- MBC, (2) in combination with palbociclib in the first-line treatment of ER+/HER2- MBC, and (3) to explore its potential in early-stage breast cancer patients in the adjuvant setting. Late last year, the Phase 3 AMEERA-5 clinical trial investigating amcenestrant in combination with palbociclib, a cyclin-dependent kinase (CDK) 4/6 inhibitor, as a first-line therapy for patients with ER+ MBC, was initiated.

A pivotal study (AMEERA-3) of amcenestrant versus physician’s choice in locally advanced or metastatic ER+ breast cancer is fully recruited. The pivotal readout is now expected in H2 2021. Of note, the trial recently passed a Data Safety Monitoring Committee (DSMC) futility analysis.

About ER+ metastatic breast cancer

MBC is breast cancer that has spread outside the mammary gland to another part of the body, such as the liver, brain, bones or lungs. It is also known as Stage IV and is the most advanced stage of breast cancer.¹ About two of every three cases of breast cancer are HR+, meaning the cancer is fueled by the hormones estrogen or progesterone.² HR+

breast cancers can be classified as ER+ and/or progesterone receptor-positive (PR+).² ER+ breast cancer accounts for approximately 75% of all breast cancers³ and is the most common type of breast cancer diagnosed today.⁴ The five-year relative survival for distant (cancer that has metastasized) female breast cancer is 28.1%.⁵ Endocrine therapies were among the first treatments to be administered for HR+ MBC and are considered standard of care in the first-line setting. However, new options are needed as resistance often emerges, limiting the effectiveness of these treatments for patients with metastatic disease over time.⁶

About the AMEERA-1 clinical trial

AMEERA-1 is an open-label, Phase 1/2, first-in-human study designed to evaluate amcenestrant as a monotherapy and in combination with targeted therapies in postmenopausal women with ER+/HER2- MBC. Parts A (dose escalation) and B (dose expansion) were designed to determine the maximum tolerated dose of amcenestrant administered as monotherapy, while Parts C and D are evaluating dose escalation and expansion for amcenestrant in combination with palbociclib to determine the recommended Phase 2 dose for the combination and to characterize its safety profile. Primary efficacy objectives include antitumor activity by ORR and CBR per RECIST v1.1 criteria, as well as characterizing the overall safety profile of amcenestrant as a monotherapy and in combination with palbociclib. Eligible patients included women with histological diagnosis of breast adenocarcinoma with locally advanced or metastatic ER+/HER2- disease and at least six months of prior exposure to endocrine therapy, including patients with early relapse while on adjuvant endocrine therapy that was initiated more than 24 months ago, or who relapsed less than 12 months after completion of adjuvant endocrine therapy.⁷

For more information on amcenestrant clinical trials, please visit www.clinicaltrials.gov.

Dr. Chandarlapaty has provided consulting services to Sanofi.

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Sanofi Media Relations Contact

Sally Bain
Tel.: +1 (781) 264-1091

Sanofi Investor Relations Contacts Paris

Eva Schaefer-Jansen
Arnaud Delepine

Sally.Bain@sanofi.com

Sanofi Investor Relations Contacts North America

Felix Lauscher
Fara Berkowitz
Suzanne Greco

Sanofi IR main line:

Tel.: +33 (0)1 53 77 45 45

investor.relations@sanofi.com

<https://www.sanofi.com/en/investors/contact>

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¹ Breastcancer.org. Metastatic Breast Cancer. https://www.breastcancer.org/symptoms/types/recur_metast. Accessed March 2021.

² American Cancer Society. Hormone Therapy for Breast Cancer. <https://www.cancer.org/cancer/breast-cancer/treatment/hormone-therapy-for-breast-cancer.html>. Accessed February 2021.

³ Sanofi Science and Innovation. Unlock a Promising Therapeutic Approach for Breast Cancer <https://www.sanofi.com/en/science-and-innovation/unlock-the-potential-of-a-promising-therapeutic-approach-for-breast-cancer>. Accessed August 2020.

⁴ Silverman, A. ER-Positive Breast Cancer: Prognosis, Life Expectancy, and More. Healthline. [https://www.healthline.com/health/breast-cancer/er-positive-prognosis-life-expectancy#:~:text=Estrogen%20receptor%2Dpositive%20\(ER%2D,cancer%20are%20hormone%20receptor%2Dpositive](https://www.healthline.com/health/breast-cancer/er-positive-prognosis-life-expectancy#:~:text=Estrogen%20receptor%2Dpositive%20(ER%2D,cancer%20are%20hormone%20receptor%2Dpositive). Accessed February 2021.

⁵ National Cancer Institute. Cancer Stat Facts: Female Breast Cancer. <https://seer.cancer.gov/statfacts/html/breast.html>. Accessed February 2021.

⁶ Kaklamani, V. G., & Gradishar, W. J. (2017). Endocrine Therapy in the Current Management of Postmenopausal Estrogen Receptor-Positive Metastatic Breast Cancer. *The oncologist*, 22(5), 507–517. <https://doi.org/10.1634/theoncologist.2015-0464>. Accessed October 2020.

⁷ ClinicalTrials.gov. Phase 1 / 2 Study of SAR439859 Single Agent and in Combination With Other Anti-cancer Therapies in Postmenopausal Women With Estrogen Receptor Positive Advanced Breast Cancer (AMEERA-1). <https://www.clinicaltrials.gov/ct2/show/NCT03284957>. Accessed April 2021.