Jazz Pharmaceuticals Presents Updated Phase 2a Data at SABCS 2023 Showcasing Potential of Zanidatamab in HER2+/HR+ Metastatic Breast Cancer

December 08, 2023

First presentation of progression-free survival (PFS) primary endpoint data show zanidatamab plus palbociclib and fulvestrant demonstrated a PFS of 67% at 6 months and a median PFS of 12 months in patients with heavily pre-treated HER2+/HR+ metastatic breast cancer (mBC)

Efficacy and safety results support further investigation of this targeted combination therapy as a potential chemotherapy-free option for patients with HER2+/HR+ mBC

DUBLIN, Dec. 8, 2023 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today presented updated data from the Phase 2a trial of investigational zanidatamab, a HER2-targeted bispecific antibody, in combination with palbociclib, a CDK4/6 inhibitor, and fulvestrant, a selective estrogen receptor antagonist, in patients with HER2-positive (HER2+)/HR-positive (HR+) metastatic breast cancer (mBC) as part of a late-breaking oral presentation at the 2023 San Antonio Breast Cancer Symposium (SABCS).

Data from 51 patients with heavily pretreated HER2+/HR+ mBC (median of 4 prior regimens in the metastatic setting) who were treated with zanidatamab plus palbociclib and fulvestrant demonstrated a progression-free survival at six months (PFS6) of 67% (n=34) [95% confidence interval: 52, 79]. Secondary endpoint findings included a median progression-free survival (mPFS) of 12 months [95% CI: 8, 15] and a confirmed objective response rate (cORR) of 35% [95% CI: 21, 50] with a median duration of response (DOR) of 15 months. The combination regimen was well tolerated with a manageable safety profile.

"Metastatic breast cancer is a particularly aggressive and devastating disease, and patients whose cancer has progressed despite numerous therapeutic interventions are in dire need of additional treatment options – particularly chemotherapy-free options," [1,2] said Santiago Escrivá-de-Romani, MD, Vall d'Hebron Institute of Oncology (VHIO), Vall d'Hebron University Hospital, and primary trial investigator. "Targeting both the HER2 and hormone receptor pathways can be a promising approach for applicable patients, and the durable responses seen in this study signal the potential for this combination to fill a persistent and much needed treatment gap among these patients."[3]

"The late-breaking data presented at SABCS for zanidatamab in combination with palbociclib and fulvestrant in HER2+/HR+ metastatic breast cancer as a chemotherapy-free treatment option in heavily pretreated patients provide yet another example of the promise this HER2-targeted bispecific antibody holds in the treatment of HER2-expressing cancers where significant unmet needs exist," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development of Jazz Pharmaceuticals. "We are encouraged by the meaningful clinical benefit seen in this trial, and we look forward to continuing to advance our broader clinical development program for zanidatamab in breast cancer and other HER2-expressing solid tumors, with the goal of addressing some of the greatest unmet needs in cancer with HER2 expression."

Trial Results

Results of the Phase 2a trial (NCT04224272) presented at SABCS indicate that zanidatamab in combination with palbociclib and fulvestrant, demonstrated meaningful PFS outcomes with a well tolerated safety profile in patients with heavily pretreated HER2+/HR+ mBC.

The single-arm trial evaluated zanidatamab plus palbociclib and fulvestrant in 51 patients with HER2+/HR+ unresectable, locally advanced or metastatic breast cancer who had received prior treatment with at least trastuzumab, pertuzumab, and T-DM1, and no prior treatment with a CDK4/6 inhibitor. Patients treated with the combination regimen received a median of four prior systemic regimens in the metastatic setting (range, 1-12).

Recommended doses of the zanidatamab plus palbociclib and fulvestrant combination therapy were determined in Part 1 of the study. The primary endpoint of Part 2 was PFS6. Other endpoints included mPFS, cORR per RECIST v1.1, DCR and DOR.

At the time of data cutoff (August 3, 2023), treatment with zanidatamab in combination with palbociclib and fulvestrant resulted in a PFS6 of 67% (n=34) and mPFS of 12 months [95% CI: 8, 15]. Median duration of follow-up was 16 months (range, 2-32). Patients treated with the combination regimen achieved a cORR of 35% and DCR of 91%.

Efficacy	**All pts (N=51)**
PFS6, n (%) (95% CI)	34 (67) (52-79)
Median PFS, mo (95% CI)	12 (8-15)
cORR, n (%) (95% CI)	16 (35) (21-50)
Confirmed best overall response (cBOR), n (%) Complete Response Partial response SD PD	 3 (6) 13 (28) 26 (56) 4 (9)
DCR, n (%) (95% CI)	42 (91) (79-98)

Median DOR, mo (95% CI)	15 (12-25)

Zanidatamab plus palbociclib and fulvestrant was well tolerated with a manageable safety profile. One serious treatment-related AE (transaminases increased) was reported (which resolved). No treatment-related deaths were reported. The most common treatment-related AEs (>20% of patients) were diarrhea, neutrophil count decrease/neutropenia, nausea, stomatitis, anemia, vomiting and asthenia. One patient discontinued the combination treatment due to an AE; three patients discontinued palbociclib due to an AE.

The abstract is available to conference registrants on the SABCS conference website here. (Abstract Number LBO1-04).

Additional data being presented at SABCS for zanidatamab include a spotlight poster presentation highlighting positive results of an investigator-sponsored Phase 1 trial evaluating neoadjuvant single-agent zanidatamab in patients with stage 1 node-negative HER2+ breast cancer (Abstract Number PS09-03).

About Zanidatamab
Zanidatamab is an investigational bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. This unique design and increased binding results in multiple mechanisms of action, including dual HER2 signal blockade, removal of HER2 protein from the cell surface, and immune-mediated cytotoxicity leading to encouraging antitumor activity in patients. Zanidatamab is being developed in multiple clinical trials as a targeted treatment option for patients with solid tumors that express HER2. Zanidatamab is being developed by Jazz and BeiGene, Ltd. (BeiGene) under license agreements from Zymeworks, which first developed the molecule.

The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy designation for zanidatamab development in patients with previously treated HER2 gene-amplified biliary tract cancers (BTC), and two Fast Track designations for zanidatamab: one as a single agent for refractory BTC and one in combination with standard of care chemotherapy for first-line gastroesophageal adenocarcinoma (GEA). Additionally, zanidatamab has received Orphan Drug designations from FDA for the treatment of BTC and GEA, as well as Orphan Drug designation from the European Medicines Agency for the treatment of BTC and gastric cancer. Zanidatamab was also granted Breakthrough Therapy designation from the Center for Drug Evaluation (CDE) in China.

In this Phase 2a trial, zanidatamab is being explored in combination with palbociclib under a clinical trial and supply agreement with Pfizer Inc.

About Jazz Pharmaceuticals
Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases—often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. Please visit www.jazzpharmaceuticals.com for more information.

Caution Concerning Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to the potential for zanidatamab in combination with palbociclib and fulvestrant to fill a persistent treatment gap among metastatic breast cancer patients and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with pharmaceutical product development, and other risks and uncertainties affecting Jazz Pharmaceuticals and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2022, as supplemented by our Quarterly Report on Form 10-Q for the quarter ended June 30, 2023, and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

Contacts:

Jazz Media Contact:
Kristin Bhavnani
Head of Global Strategic Brand Engagement
Jazz Pharmaceuticals plc
CorporateAffairsMediaInfo@jazzpharma.com
Ireland +353 1 637 2141
U.S. +1 215 867 4948

Jazz Investor Contact:
Andrea N. Flynn, Ph.D.
Vice President, Head, Investor Relations
Jazz Pharmaceuticals plc
investorinfo@jazzpharma.com
Ireland +353 1 634 3211
U.S. +1 650 496 2717

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