23andMe Therapeutics Announces Phase 2 Results for Two Additional Cancer Cohorts and Correlative Biomarker Data from 23ME-00610 Study

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23ME-00610 monotherapy demonstrates preliminary evidence of clinical benefit in clear-cell renal-cell carcinoma, with one confirmed partial response

Higher tumor expression of CD200 and human genetics correlated with increased clinical benefit, suggesting potential value as patient selection biomarkers

Greater response in "cold" tumors suggests opportunity in patients unable to benefit from PD-1/PD-L1 checkpoint inhibitors

SUNNYVALE, Calif., Sept. 15, 2024 (GLOBE NEWSWIRE) -- 23andMe Holding Co. (Nasdaq: ME) ("23andMe"), a leading human genetics and biopharmaceutical company, announced positive preliminary Phase 2 safety and efficacy data from its Phase 1/2a clinical trial covering two new patient cohorts from 23ME-00610 ('610), a first-in-class anti-CD200R1 antibody, at the European Society of Medical Oncology (ESMO) Congress 2024 in Barcelona, September 13-17.

23andMe Therapeutics presented posters summarizing results for 10 patients with clear-cell renal-cell carcinoma (ccRCC) and for 13 patients with tumor mutational burden-high (TMB-H) or microsatellite instability-high (MSI-H) cancers. A third poster summarized data from 118 participants across the Phase 1/2a trial to evaluate high tumor expression of CD200 as a potential predictive biomarker of clinical benefit. These presentations supplement data for cohorts with neuroendocrine and ovarian cancer presented earlier this year at the 2024 American Society of Clinical Oncology Meeting. (The 23andMe ESMO posters are available on the 23andMe Therapeutics and Investor websites).

"We continue to be encouraged by evidence for therapeutic potential, in the form of multiple patients with durable clinical benefit from '610," said Jennifer Low, M.D., Ph.D., Head of Therapeutics Development, 23andMe. "Furthermore, the emergence of CD200 expression as a candidate biomarker has the potential to give us a powerful tool for patient selection. The progress we have made to date suggests that interrupting the CD200/CD200R1 pathway has great potential to reverse immune suppression in the tumor microenvironment and to help cancer patients who have progressed after multiple lines of treatment, including existing checkpoint inhibitors."

23ME-00610 is a first-in-class IgG1 antibody designed to reverse immunosuppression by inhibiting binding of CD200R1 on immune cells with CD200 on tumor cells. In preclinical studies, this mechanism leads to restoration of T cell activity and killing of CD200-expressing tumor cells. The CD200R1 axis was recognized as a potentially significant checkpoint inhibition pathway through the identification of pleiotropic causal variants with opposing effect on risk for cancer and immune diseases, referred to by 23andMe Therapeutics as an immuno-oncology signature.

Key Takeaways:

- Confirmed partial response (38% decrease in measured tumor burden) in a patient with refractory ccRCC (>11 cycles at data cut-off).
- 23ME-00610 monotherapy continues to demonstrate acceptable safety and tolerability, and achieves the prespecified targets for maximal pharmacology at 1400 mg dosed every three weeks.
- Higher tumor expression of CD200 may be associated with clinical benefit in some patient groups treated with 23ME-00610, warranting further exploration of this biomarker.
- In addition to CD200 expression, histology data suggest that immunosuppressed ("cold") tumors may be more likely to exhibit disease control with 23ME-00610. Biopsied patients that had tumor shrinkage or prolonged stable disease with 23ME-00610 treatment tended to be less inflamed at baseline and have lower levels of immunosuppressive (M2) macrophages.
- Emerging data demonstrate the potential interaction of a tumor biomarker with host genetics, leveraging 23andMe developed polygenic risk scores.

Further details - ccRCC cohort

- Between June 5 and December 12, 2023, ten adult patients with advanced ccRCC who received a median of four prior treatment lines (range: 2-7) were enrolled and received a median of three cycles (range: 2-12) of 23ME-00610, with three patients remaining on study at the July 1, 2024 data cutoff.
- In a 61 year old male, a confirmed partial response and ongoing treatment duration > 32 weeks for a treatment of refractory kidney cancer with high CD200 tumor expression was observed.
- The safety and tolerability profile remains acceptable and promising for potential anti-cancer combinations in ccRCC patients.
    - No treatment-emergent adverse events (TEAEs) leading to 23ME-00610 dose interruption or discontinuation were reported.
    - Related treatment-emergent adverse events (TEAEs) occurred in three patients (30%); all were G1/G2, were reported once each (10%), and included dry mouth, nausea, constipation and vomiting.

- Preliminary baseline tumor data may suggest that highly vascularized tumors with high CD200 associates with benefit from 23ME-00610 treatment.

Further details – TMB-H/MSI-H cohort

- Between June 20, 2023 and April, 2024, 13 adult patients with locally advanced or metastatic TMB-H (N=11; 84.6%) and/or MSI-H (N=5; 38.5%) solid cancers who received a median of five prior treatments (range 3-11; prior immunotherapy in 84.6%) were enrolled and received a median of three cycles of 23ME-00610 (range 1-11), and 1 patient remaining on study at the July 1, 2024 data cutoff.

Further details – CD200 biomarker

- Between January 2022 and April 2024, 118 adult patients with locally advanced and metastatic solid tumors were enrolled in the Phase 1/2a clinical trial for 23ME-00610. Archival tissue and genotyping was requested from all patients, and some subsets of patients received baseline and on-treatment biopsies.
- Higher tumor cell expression of CD200 associates with 23ME-00610 in some patients, and is further augmented if combined with genetic based host immune set point readouts (e.g. autoimmune hypothyroidism polygenic risk score), warranting further exploration of this and other biomarkers for potential future patient selection.
- Neuroendocrine tumors that had tumor shrinkage or prolonged stable disease tended to be less inflamed at baseline, though potentially more permissive to immune activation due to lower macrophage to lymphocyte ratio.
- Analysis of pre- and on-treatment tumor samples showed an increase in T and NK cell markers and an increase in interferon inducible genes with 23ME-00610 treatment suggesting pharmacodynamic immune modulation.

About 23ME-00610
23ME-00610 is a monoclonal antibody that binds to CD200R1 to prevent the interaction of CD200R1 with CD200. Using the world's largest proprietary database of health and genetic information, 23andMe identified genetic variants of CD200R1, CD200, and DOK2, the downstream signaling protein, associated with higher risks of immune disease and lower risks of cancer, pinpointing CD200R1 as a promising immuno-oncology target. Additional preclinical data validated the CD200-CD200R1 pathway as an immune checkpoint, and potential target for reversing immune tolerance in cancer as a monotherapy, or in combination with other therapies. Clinical data from the dose escalation cohort of patients with advanced solid tumors has shown 23ME-00610 has favorable pharmacokinetics (PK) for dosing once every three weeks, expected on-target pharmacologic activity, and a promising safety and tolerability profile.

About 23andMe
23andMe is a genetics-led consumer healthcare and biopharmaceutical company empowering a healthier future. For more information, please visit https://therapeutics.23andme.com.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, including. All statements, other than statements of historical fact, included or incorporated in this press release are forward-looking statements. The words "believes," "anticipates," "estimates," "plans," "expects," "intends," "may," "could," "should," "potential," "likely," "projects," "predicts," "continue," "will," "schedule," and "would" or, in each case, their negative or other variations or comparable terminology, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are predictions based on 23andMe's current expectations and projections about future events and various assumptions. 23andMe cannot guarantee that it will actually achieve the plans, intentions, or expectations disclosed in its forward-looking statements and you should not place undue reliance on 23andMe's forward-looking statements. These forward-looking statements involve a number of risks, uncertainties (many of which are beyond the control of 23andMe), or other assumptions that may cause actual results or performance to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements contained herein are also subject generally to other risks and uncertainties that are described from time to time in the Company's filings with the Securities and Exchange Commission, including under Item 1A, "Risk Factors" in the Company's most recent Annual Report on Form 10-K, as filed with the Securities and Exchange Commission, and as revised and updated by our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. The statements made herein are made as of the date of this press release and, except as may be required by law, 23andMe undertakes no obligation to update them, whether as a result of new information, developments, or otherwise.

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