

## CureVac's CVGBM Cancer Vaccine Induces Promising Immune Responses in Phase 1 Study in Glioblastoma Presented at the ESMO 2024 Congress

- Preliminary immunogenicity results demonstrate induction of cancer antigen-specific T-cell responses in 77% of evaluable patients following CVGBM monotherapy
- 84% of immune responses were *de novo*, observed in patients without pre-existing T-cell activity against encoded cancer antigens
- CVGBM was generally well tolerated up to the highest tested dose level of 100 µg with no dose-limiting toxicities
- Most common adverse events were mild to moderate systemic reactions such as headache, fever and chills, which resolved within 1–2 days post injection
- 100 µg was selected as the recommended dose for the dose expansion phase, which recently started enrollment

**TÜBINGEN, Germany/BOSTON, USA – September 13, 2024** – CureVac N.V. (Nasdaq: CVAC) (“CureVac”), a global biopharmaceutical company developing a new class of transformative medicines based on messenger ribonucleic acid (“mRNA”), today presented compelling data from the dose-escalation Part A of its ongoing Phase 1 CVGBM cancer vaccine study in patients with glioblastoma at the European Society for Medical Oncology (ESMO) Congress. The presented data include safety, tolerability and initial immunogenicity data provided for all evaluable patients treated within Part A of the trial with CVGBM dose levels of 12-100 µg. The presentation can be reviewed [here](#).

In this highly aggressive and challenging cancer indication, preliminary immunogenicity results demonstrate that treatment with CVGBM-only following chemo-radiation therapy successfully induces cancer antigen-specific T-cell responses in 77% of evaluable patients. Most notably, within the group of responding patients, 84% of immune responses were generated *de novo* by the CVGBM vaccination, inducing T-cell activity in patients who had no pre-existing T-cell activity against the encoded antigens. While CD8<sup>+</sup> T-cells primarily attack and destroy cancer cells, CD4<sup>+</sup> T-cells play a critical role in coordinating the immune response and supporting the activity of CD8<sup>+</sup> T-cells over time. The majority of responding patients (69%) showed cancer antigen-specific CD8<sup>+</sup> responses, 31% of responding patients had CD4<sup>+</sup> responses and 23% had both a CD8<sup>+</sup> and a CD4<sup>+</sup> response.

“These early data are encouraging. Most importantly, the strong *de novo* T-cell responses seen in a significant number of patients reflect the vaccine’s ability to break through immune tolerance to the tumor and generate a new immune response,” said Prof. Dr. Ghazaleh Tabatabai, Chair, Department of Neurology & Interdisciplinary Neuro-Oncology, University Hospital Tübingen and Hertie Institute for Clinical Brain Research. “The CVGBM safety profile is acceptable, and we are eager to see these results further validated in the next phase of the study. This could mark an important moment in the fight against this devastating disease.”

CureVac's Chief Scientific Officer, Dr. Myriam Mendila, added: "These first-in-human data highlight for the first time the broader potential of our second-generation mRNA backbone in cancer immunotherapy. The ability of CVGBM to elicit both CD8<sup>+</sup> and CD4<sup>+</sup> *de novo* T-cell responses suggests that the vaccine is enhancing the immune system's capacity for a coordinated defense against the cancer. As we conduct the next phase of the trial, we are building a strong foundation for future shared antigen as well as personalized cancer vaccines across different tumor types that could offer significant benefits to patients."

Immune activation was accompanied by a favorable safety and tolerability profile, with no dose-limiting toxicities observed up to and including the highest tested dose of 100 µg, as confirmed by an independent Data and Safety Monitoring Board. The majority of treatment-related adverse events (TRAEs) were reported as grade 1 (mild) and grade 2 (moderate) systemic reactions characteristic to mRNA-based therapeutics. These included headache, chills, fever and fatigue, which resolved within 1-2 days following the injection. Seven patients reported a total of nine grade 3 (severe) TRAEs, of which four were classified as serious adverse events (SAEs). No grade 4 or 5 adverse events occurred. Correspondingly, a 100 µg dose was selected as the recommended dose for the already initiated dose-confirmation Part B of the study.

The open-label study is evaluating the safety and tolerability of CVGBM in HLA-\*02:01-positive patients with newly diagnosed and surgically resected MGMT-unmethylated glioblastoma or astrocytoma with a molecular signature of glioblastoma. CVGBM replaces the temozolomide maintenance phase. It is administered as a monotherapy after surgical resection and completion of radiotherapy with or without chemotherapy. The study consists of two parts, a dose-escalation part (Part A) and a dose-expansion part (Part B). In the fully enrolled Part A, patients received seven intramuscular vaccinations at escalating doses in the range of 12 to 100 µg on days 1, 8, 15, 29, 43, 57 and 71 and optional maintenance vaccinations in case of non-progression or potential benefit. 16 patients were enrolled, of which 13 were evaluable for immune responses. All patients completed surgery, 44% with complete tumor resection and 56% with only partial resection followed by chemo-radiation with temozolomide. Antigen-specific CD4<sup>+</sup> and CD8<sup>+</sup> T-cell responses were assessed at relevant pre-determined timepoints until day 99. Part B of the study is currently ongoing at the recommended dose of 100 µg.

More information can be found at [clinicaltrials.gov \(NCT05938387\)](https://clinicaltrials.gov/ct2/show/study/NCT05938387).

### **About CVGBM**

Based on CureVac's proprietary second-generation mRNA backbone, designed for improved mRNA translation, increased protein expression and optimized induction of T-cell responses, CVGBM encodes a single fusion protein comprising eight epitopes derived from four tumor-associated antigens (TAA) with relevance in glioblastoma, including five HLA class I (HLA-\*02:01) epitopes and three class II epitopes. CVGBM applies unmodified mRNA and is formulated within lipid nanoparticles (LNPs). The Phase 1 proof-of-principle study of CVGBM is currently being conducted in Germany, Belgium and the Netherlands.

## About CureVac

CureVac (Nasdaq: CVAC) is a pioneering multinational biotech company founded in 2000 to advance the field of messenger RNA (mRNA) technology for application in human medicine. In more than two decades of developing, optimizing, and manufacturing this versatile biological molecule for medical purposes, CureVac has introduced and refined key underlying technologies that were essential to the production of mRNA vaccines against COVID-19, and is currently laying the groundwork for application of mRNA in new therapeutic areas of major unmet need. CureVac is leveraging mRNA technology, combined with advanced omics and computational tools, to design and develop off-the-shelf and personalized cancer vaccine product candidates. It also develops programs in prophylactic vaccines and in treatments that enable the human body to produce its own therapeutic proteins. Headquartered in Tübingen, Germany, CureVac also operates sites in the Netherlands, Belgium, Switzerland, and the U.S. Further information can be found at [www.curevac.com](http://www.curevac.com).

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For further information, please reference the company's reports and documents filed with the U.S. Securities and Exchange Commission (SEC). You may get these documents by visiting EDGAR on the SEC website at [www.sec.gov](http://www.sec.gov).