



Checkmate Pharmaceuticals Presents Positive Clinical Data with CMP-001 at The 34th Annual Meeting of The Society for Immunotherapy of Cancer (SITC)

Objective response rate (ORR) of 25% and duration of response of 16.9+ months observed with CMP-001 in combination with pembrolizumab in patients with anti-PD-1 refractory melanoma

Major pathological response rate (MPR) of 71% observed in a trial of neoadjuvant CMP-001 in combination with nivolumab in patients with high-risk, resectable melanoma

Monotherapy responses to CMP-001 observed in patients with anti-PD-1 refractory melanoma

CAMBRIDGE, Mass., November 5, 2019 – [Checkmate Pharmaceuticals Inc. \(Checkmate\)](#), a clinical stage biopharmaceutical company focused upon activation of innate immunity to treat cancer, today announced the presentation of new data from two ongoing clinical trials evaluating CMP-001, Checkmate’s Toll-like receptor 9 (TLR9) agonist, in combination with the anti-PD-1 therapies pembrolizumab (KEYTRUDA®) or nivolumab (OPDIVO®), in patients with melanoma.

“CMP-001 is a differentiated TLR9 agonist that activates a tumor-specific T cell response. When combined with checkpoint inhibitors, CMP-001 can induce deep and durable systemic anti-tumor responses,” said Dr. Art Krieg, Checkmate’s Founder and CSO. “These clinical data reaffirm the potential for CMP-001 to enhance responsiveness or overcome resistance to immune checkpoint inhibitors. We look forward to the next stages of development with this program, including evaluation in other cancers.”

Durable responses in anti-PD-1 refractory melanoma following intra-tumoral injection of a Toll-like receptor 9 (TLR9) agonist, CMP-001, in combination with pembrolizumab (Abstract #: 11548/O87)

On Friday, November 8, 2019 at 12:15pm ET, Dr. John M. Kirkwood, Usher Professor of Medicine and Dermatology, University of Pittsburgh School of Medicine, and Co-Director, Melanoma and Skin Cancer Program, University of Pittsburgh Cancer Institute and UPMC Hillman Cancer Center, is presenting late-breaking data from a Checkmate-sponsored clinical trial of CMP-001, either in combination with pembrolizumab or as monotherapy ([NCT02680184](#)).

Updated data from the trial demonstrated that the combination of CMP-001 and pembrolizumab continued to be well tolerated, with an objective response rate (ORR) of 25% according to RECIST v1.1 criteria. The study treatment induced deep and durable systemic anti-tumor responses in patients with melanoma who previously progressed on anti-PD-1 treatments; with a current Kaplan Meier estimate of median duration of response of 16.9+ months for the 28 RECIST v1.1 responders.

“These current data suggest that CMP-001 might expand the patient population that benefits from anti-PD-1 therapies,” said Dr. Kirkwood. “Most patients with cancer have non-inflamed tumor microenvironments that do not respond to checkpoint inhibitors. These trial data demonstrate that combining CMP-001 with pembrolizumab could induce an immune response against the cancer, forming a potentially effective treatment option for patients with advanced melanoma who are not responsive to anti-PD-1-based treatment regimens.”

Data were presented on the intent to treat (ITT) population of 144 patients receiving combination therapy with CMP-001 and pembrolizumab. Two formulations of CMP-001 were evaluated, either 0.01% polysorbate 20 (PS20, N=83) or 0.00167% PS20 (N=61). The lower concentration of PS20 was found to be less effective. Data were also presented on 24 patients who received CMP-001 monotherapy.

Key highlights from these clinical data include:

CMP-001 in combination with pembrolizumab

- The RECIST ORR in patients who received the 0.01% PS20 formulation was 25% (21/83; 95% confidence interval 16%-36%), including 6 complete responses and 15 partial responses.
- Four additional patients who continued study therapy beyond initial disease progression achieved a partial or complete response.
- The Kaplan Meier estimate for median duration of response is 16.9+ months [95% CI=5.8, not reached] in the 28 RECIST responders and 25.2+ months [95% CI=8.6, not reached] when including the additional 4 patients with post-progression responses. The median duration of response has not been reached.
- Among responding patients, non-injected target lesions regressed by a similar magnitude to injected target lesions.
- In the ITT population, the most common treatment-related adverse events were flu-like symptoms, including chills, fever, fatigue, nausea, vomiting and headache for patients receiving combination treatment. Six patients (4%) discontinued study therapy due to treatment-related adverse events.

CMP-001 monotherapy

- Of the 24 patients treated with CMP-001 monotherapy, 5 patients achieved a partial response. Responses were less durable compared to those for patients receiving CMP-001 in combination with pembrolizumab.

Phase II Trial of neoadjuvant nivolumab (Nivo) and intra-tumoral (IT) CMP-001 in high risk resectable melanoma (MEL): Preliminary Results (Abstract #: 11648/O34)

On Saturday, November 9, 2019 at 6:15pm ET, Dr. Diwakar Davar, Assistant Professor of Medicine at the University of Pittsburgh School of Medicine, is presenting data from an investigator-sponsored trial evaluating neoadjuvant treatment with CMP-001 in combination with nivolumab in patients with Stage IIIB/C/D Melanoma ([NCT03618641](https://clinicaltrials.gov/ct2/show/study/NCT03618641)).

Preliminary data from the trial show that neoadjuvant IT CMP-001 in combination with nivolumab in PD-1 naïve patients was generally well tolerated with no dose limiting toxicities or delays in surgery related to the neoadjuvant treatment. A major pathologic response rate (MPR) of 71% (15/21) was reported in 21 evaluable patients to date. Of the 15 responding patients, 13 patients had a pathological complete response (pCR). These data suggest that the addition of IT CMP-001 may increase the clinical efficacy of PD-1 blockade. Furthermore, translational studies demonstrated that the combination augmented peripheral blood and intra-tumoral anti-melanoma CD8+ T cell immune responses.

“The preliminary results of our study show that a combination treatment with neoadjuvant nivolumab and CMP-001 is associated with high rates of major pathologic response, including a remarkable proportion of subjects with complete pathological response,” said Dr. Davar. “Moreover, the combination treatment has a favorable toxicity profile. We look forward to evaluating the effect of the treatment upon post-surgical relapse as the data mature.”

About Checkmate's Phase 1b Study (CMP-001-001)

CMP-001-001 (NCT02680184) is an ongoing, multicenter two-part, open label Phase 1b clinical study in advanced melanoma. The study is being conducted at 13 sites in the USA.

The primary objective of Part 1 of the study is to determine the recommended phase 2 dose (RP2D) of CMP-001 when given in combination with pembrolizumab in PD-1 resistant patients. Secondary objectives are to assess the safety and efficacy of CMP-001 when given in combination with pembrolizumab, and to assess the pharmacodynamic effects of the addition of CMP-001 to pembrolizumab on serum concentrations of CXCL10 (IP-10).

Part 1 of the study utilized a dose escalation scheme to identify the RP2D and schedule. During dose escalation, patients were enrolled to cohorts of ≥ 3 patients at CMP-001 doses of 1, 3, 5, 7.5, and 10 mg CMP-001 in two dosing schedules (weekly for 7w, followed by q3w; or weekly for 2w, followed by q3w).

In the Part 1 dose expansion, two formulations of CMP-001 were evaluated, either with 0.01% polysorbate (PS20) or with 0.00167% PS20. The CMP-001 0.01% PS20 formulation, 10 mg dose, with a weekly dosing schedule for 7w, followed by q3w dosing, was selected for further development.

Part 2 of the study continues to enroll and is evaluating the safety and efficacy of CMP-001 administered as monotherapy at the same dose, schedule and formulation selected for further development in Part 1 of the study.

About CMP-001

CMP-001 is a first-in-class CpG-A Toll-like receptor 9 (TLR9) agonist that is encapsulated in a virus-like particle. CMP-001 is designed to induce both innate and adaptive anti-tumor immune responses, thereby converting immunologically "cold" tumors into immunologically "hot" tumors, with the potential to mediate tumor regression. It is the only CpG-A class TLR9 agonist in clinical trials and differs from other CpG classes in clinical development by having a native DNA backbone that induces the highest levels of type I Interferon (IFN). Based on analyses of gene expression in human tumors showing that increased IFN and related immune gene expression is associated with better response to PD-1 inhibition, it is believed that this mechanism of action may restore, enable or improve responses to anti-PD-1/PD-L1 therapeutics. CMP-001 is being evaluated in multiple tumor types to assess safety, activity, alternative routes of administration and combination with other immunotherapies and modalities. For information on CMP-001 trials that are currently recruiting patients, please visit www.clinicaltrials.gov.

About Checkmate Pharmaceuticals

Checkmate Pharmaceuticals is a clinical stage company that is leveraging its expertise in the field of CpG oligonucleotides to discover and develop immunotherapies designed to increase the efficacy of existing immunotherapies and to provide new treatment options for patients and their healthcare providers. Checkmate's lead product candidate, CMP-001, is an investigational cancer immunotherapeutic that has been shown to reverse resistance to PD-1 therapy in some patients. Checkmate is a privately held company headquartered in Cambridge, MA. Additional information regarding Checkmate is available at www.checkmatepharma.com.

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