Data on Anti-4CB1 Published in Molecular Cancer Therapeutics Journal

- Paper describes dual blocking mode of action of Anti-4CB1 of two molecules, BTLA and CD160, thereby unmasking solid tumors from the immune system
- Potential as a combination therapy as well as a monotherapy; activates both adaptive and innate immune responses
- Activity in real patient tumor tissue in different cancer types, with the strongest effects seen in melanoma, colon, ovarian and renal cancers
- Differential levels of blood circulating soluble HVEM (Herpes Virus Entry Mediator, or TNFRSF14) between responders and non-responders to Anti-4CB1 suggests possible companion biomarker for patient stratification

London and Israel – 20 August 2026: 4C Biomed, a biotechnology company developing novel immunotherapeutic monoclonal antibodies, has had its preclinical data set on its lead asset, anti-4CB1, published in the prestigious journal, *Molecular Cancer Therapeutics*. The paper describes its action as a novel selective HVEM-blocking antibody, which enhances T-cell and macrophage immunity against solid tumors.

The full article is entitled "*Anti-4CB1: A Novel Selective HVEM-Blocking Antibody Enhancing T-Cell and Macrophage Immunity Against Solid Tumors"* and it can be read HERE.

Checkpoint inhibitors, such as anti-PD1 (Keytruda®, Opdivo®), have transformed cancer treatment for many subsets of patients with common tumors. However, many cancers do not respond, and of those that do, the majority eventually progress. Treatment options for these patients are limited.

4C Biomed's article introduces its Anti-4CB1, a fully human monoclonal antibody against HVEM (Herpes Virus Entry Mediator, or TNFRSF14), a novel immune checkpoint which is highly expressed in malignant cancer cells across multiple cancers, including melanoma, renal, ovarian, colorectal, endometrial and hepatocellular carcinoma.

HVEM acts as a brake on the immune system through two inhibitory partner molecules, BTLA and CD160. Anti-4CB1 blocks both of these molecules resulting in a much more powerful immune response than blocking either molecule alone. Anti-4CB1 binds HVEM with high affinity; screened against c.6,000 human membrane proteins, HVEM was the only protein it bound, which is highly significant for predicting side effects down the line.

Key features of the published anti-4CB1 data and details of the study:

- **Activating higher adaptive and innate immune responses:** Anti-4CB1 increased killing of melanoma cells by patients' own tumor-infiltrating lymphocytes by 48%, the same magnitude as anti-PD1, and raised the markers that indicate T-cell activation. Control experiments confirmed the antibody is not itself toxic to tumor cells; it works by mobilizing the immune system. Combined with anti-PD1, anti-4CB1 increased macrophage-mediated destruction of tumor cells by 168%.

- **Action in real patient tumors in different cancer types:** Using 49 freshly collected patient tumor samples spanning multiple cancer types, Anti-4CB1 boosted tumor-cell killing in 28.5% of cases, compared with 14.3% for anti-PD1 alone. The headline finding was that nine of the responding samples responded to Anti-4CB1 but not to anti-PD1. Activity was strongest in melanoma, colon, ovarian and renal cancers.
- **Potential as a monotherapy or in combination:** In colon cancer and melanoma *in vivo* models, Anti-4CB1 slowed tumor growth as a monotherapy. When combined with anti-PD1, it achieved 95% tumor growth inhibition. Animals in the combination group were still alive when the study ended - they outlived the anti-PD1-only group by a statistically significant margin (p=0.03); in the combination group 80% were still alive while in the PD1 only group, only 40% remained alive. All treatments were well tolerated, with no weight loss or observed adverse events.
- **Blood-based HVEM - a possible companion test:** Melanoma patients who were treated in the clinic with anti-PD1 and responded, had significantly higher HVEM levels in their tumors before treatment began (p=0.004). Separately, in ex-vivo experiments, samples from patients with high levels of soluble HVEM circulating in their blood were less likely to respond to Anti-4CB1. This data suggest HVEM could be a viable biomarker for identifying which patients are most likely to benefit from the immuno-therapy.

Gilli Galore-Haskel, VP R&D of 4C Biomed and one of the lead authors on the paper, said:

"We are proud to publish this data today in such a prestigious journal. Very few preclinical programs are supported by such a range of data based on this many fresh human tumors samples across this many cancer types. Anti-4CB1 showed activity in patient samples where anti-PD1 was ineffective and also boosted its impact when used in combination. Data confirms that the antibody has a clean safety profile and these data show that it works by mobilizing both strands of the immune system – a powerful double action. Finally, data demonstrate that blood-based HVEM could be a valuable biomarker to assess whether patients will respond to Anti-4CB1 or not; a potential companion test is an increasing must-have feature for next generation immuno-oncology therapeutics.

"Taken together, this preclinical dataset supports advancing our anti-4CB1 programme into the clinic as soon as possible, which is our intention in the new year."

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Notes to Editors

About 4C Biomed

4C Biomed is an immune-oncology company focused on unlocking novel immune targets through its proprietary screening platform. Its lead programme is an anti-4CB1, a first-in-class, fully human monoclonal antibody targeting HVEM, a novel immune checkpoint which is highly expressed in malignant cancer cells across multiple cancers, including melanoma, renal, ovarian, colorectal, endometrial and hepatocellular carcinoma. Data shows that anti-4CB1 is active in tumors that have progressed on first-generation PD-1/L1 inhibitors, active in "cold" tumors unresponsive to PD-1/L1 therapy and enhances the activity of those drugs in combination.

The Company was spun out of Sheba Medical Center. The headquarters are located in London and its R&D is based in Israel. For more information, please visit the website: www.4CBiomed.com.

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