by CD8 lymphocytes and decreasing T Reg cells. CXD101 has been shown in a Phase I study conducted in the UK to have anti-tumour activity as monotherapy, and to be generally well tolerated.The anti-tumour efficacy of CXD101 has been investigated as monotherapy or in combination with the immune checkpoint inhibitors, anti-mouse PD-1 and anti-mouse CTLA4, respectively, in the syngeneic MSS Colon 26 model. The tumour Colon26 celles were implanted subcutaneously in immunocompetent BALB/c mice. The syngeneic tumour was seen to respond poorly to anti-PD1 and anti-CTLA4 immune therapeutics alone. As a single agent, CXD101 caused modest inhibition of tumour growth. In contrast, when administered in combination with anti-PD1 or anti-CTLA4, synergistic anti-tumour activity was observed at well tolerated doses.The CAROSELL clinical trial is testing the effect of CXD101 with nivolumab in MSS colorectal cancer, with the hypothesis that this combination will re-engage recognition of tumours by the immune system.

Trial design: The selected study population were patients with advanced or metastatic MSS CRC, previously threated with at least two lines of therapy; and ECOG PS 0, 1, or 2. A total of 5 UK investigators are contributing subjects to the study, the first of which was treated in July 2018. The design began with a Phase Ib variable dose safety run-in (n = 9). No dose-limiting toxicities were observed, and CXD101 20mg bid in combination with nivolumab 240mg was selected as the Phase II treatment.The primary objective of the Phase II element is to assess immune Disease Control Rate, as determined by CT scan tumour measurements (iRECIST), following a Simon 2-Stage statistical approach. Secondary objectives are to determine 20-week immune-related progression-free survival; overall survival; immune Objective Response Rate, and safety. The CAROSELL Study will recruit a total of 55 subjects.

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666TiP A phase Ib/ II trial to assess the safety and efficacy of CXD101 in combination with the PD-1 inhibitor nivolumab in patients with metastatic, previously-treated, microsatellite-stable (MSS) colorectal carcinoma (short title CAROSELL)

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Background: CXD101 is a histone–deacetylase inhibitor which reactivates the patient's immune system by increasing tumour expression of MHC I & II, tumoural infiltration