DEVELOPMENT OF MPDL3280A, AN ANTI-PD-L1 ANTIBODY ENGINEERED FOR ENHANCED EFFICACY AND SAFETY

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Programmed Death-Ligand 1 (PD-L1) is the predominant ligand that binds Programmed Death-1 (PD-1), an inhibitory receptor expressed on T cells following T-cell activation. PD-L1 is highly expressed in many human tumors and elevated expression is often associated with a worse prognosis. PD-L1 exerts an immune suppressive signal through binding to PD-1 and B7.1, and tumor expression of PD-L1 can mediate cancer immune evasion. Therefore, inhibition of PD-L1 binding represents an attractive strategy to restore tumor-specific T-cell immunity.

MPDL3280A is a human monoclonal antibody engineered to optimize efficacy and safety through a modification in the Fc region of the antibody. MPDL3280A targets PD-L1, inhibiting interaction with its receptors that include PD-1 and B7.1. In pre-clinical models, inhibition of PD-L1 can lead to durable anti-tumor activity. Studies evaluating the efficacy, safety and biomarker associations for MPDL3280A as a single agent and in combination with other targeted therapies will be discussed.