Plasmodium vivax is the most widespread species of malaria in humans globally and is increasingly understood to cause clinical disease in endemic areas of Southeast Asia and South America. However, vaccine development is hindered by the lack of a long-term culture system. The closely related zoonotic parasite, *Plasmodium knowlesi*, has been adapted to culture in human erythrocytes, offering an *in vitro* model which shares many common invasion pathways with *P. vivax.* High efficiency CRISPR/Cas9 genome editing in this system allows us to study *P. vivax* blood-stage vaccine targets via orthologue replacement, as well as improving understanding of *P. knowlesi* invasion biology in its own right. Previous work in this system demonstrated sequential roles for two essential *P. knowlesi* invasion proteins, with normocyte binding protein Xa (NBPXa) required for erythrocyte deformation followed by Duffy binding protein α (PkDBPα) binding DARC to trigger a Ca^{2+} flux and merozoite reorientation. These proteins are part of larger families essential to invasion shared across *Plasmodium spp.*: the reticulocyte binding-like/reticulocyte binding homologous proteins (RBLs/RHs, including NBPXa), and the Duffy binding/erythrocyte binding-like proteins (EBLs, including PkDBPα). *P. vivax* is believed to follow a similar stepwise invasion process, using a repertoire of RBLs and the homologous PvDBP. Both parasite species lack functional redundancy for DBP-DARC binding in human infection, so PvDBP is a prime vaccine target. However, increasing reports of *P. vivax* infections in $Duffy^{neg}$ individuals raise concerns around monovalent DBP-based vaccines, so other essential blood-stage antigens must be urgently explored for use alongside (or instead of) DBP. In this work, we demonstrate that NBPXa-targeting antibodies inhibit *P. knowlesi* growth in culture, and combined inhibition with DBP shows potential synergistic activity. Additionally, we have generated a transgenic *P. knowlesi* line which enables conditional NBPXa complementation. This allows us to examine the role of gene copy number on invasion efficacy, how polymorphisms affect antibody mediated inhibition, and the role of the various *P. vivax* RBLs. For example, the mechanism of reticulocyte restriction in *P. vivax* has not been confirmed, but PvRBP2b and 2a have each been highlighted as potential mediators. This transgenic line could help to study these proteins during invasion and identify specific PvRBLs to prioritise for combined vaccine approaches.