

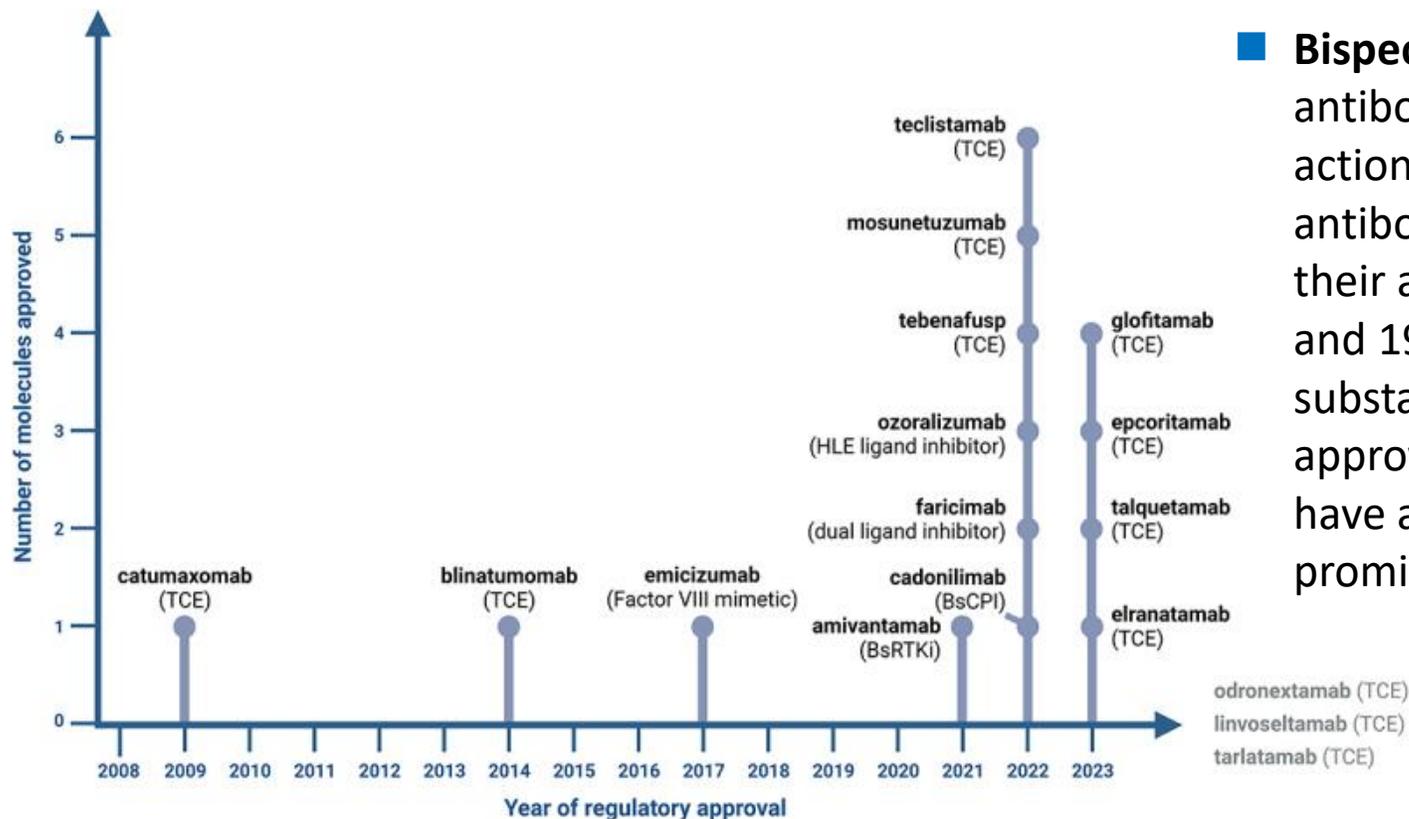
Evaluation of Bispecific Antibody in NHP



2024.09

OncoWuXi Newsletter

Introduction of bispecific antibodies (bsAbs)



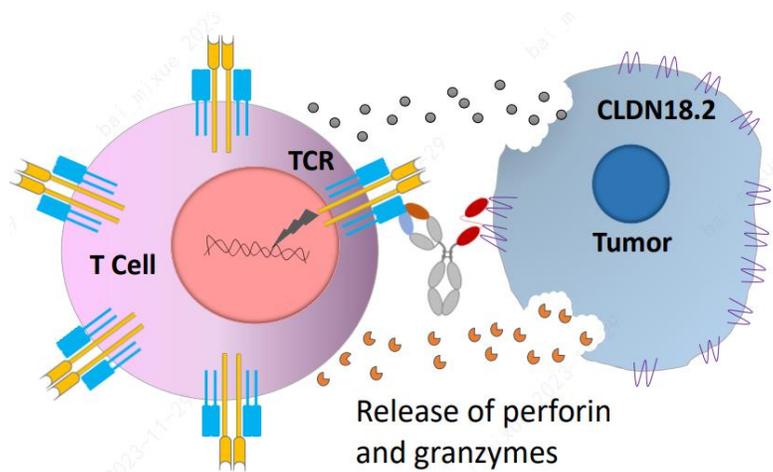
■ **Bispecific antibodies (bsAbs)** are a class of antibodies that can mediate novel mechanisms of action compared to monospecific monoclonal antibodies (mAbs). Since the discovery of mAbs and their adoption as therapeutic agents in the 1980s and 1990s, the development of bsAbs has held substantial appeal. Notably, of the 13 currently approved bsAbs, two, emicizumab and faricimab, have achieved blockbuster status, showing the promise of this novel class of therapeutics.

MAbs. 2024 Jan-Dec;16(1):2321635. doi: 10.1080/19420862.2024.2321635.

Study summary

Due to the similarities in the pharmacokinetics and pharmacodynamics (PKPD) with human, non-human primates (NHPs) are often used in preclinical researches to predict the dose-effect relationship in human, and therefore the dose level to be tested in first-in-human trials. Herein, we showcase a case study evaluating PK/PD and safety of a bsAb in NHP.

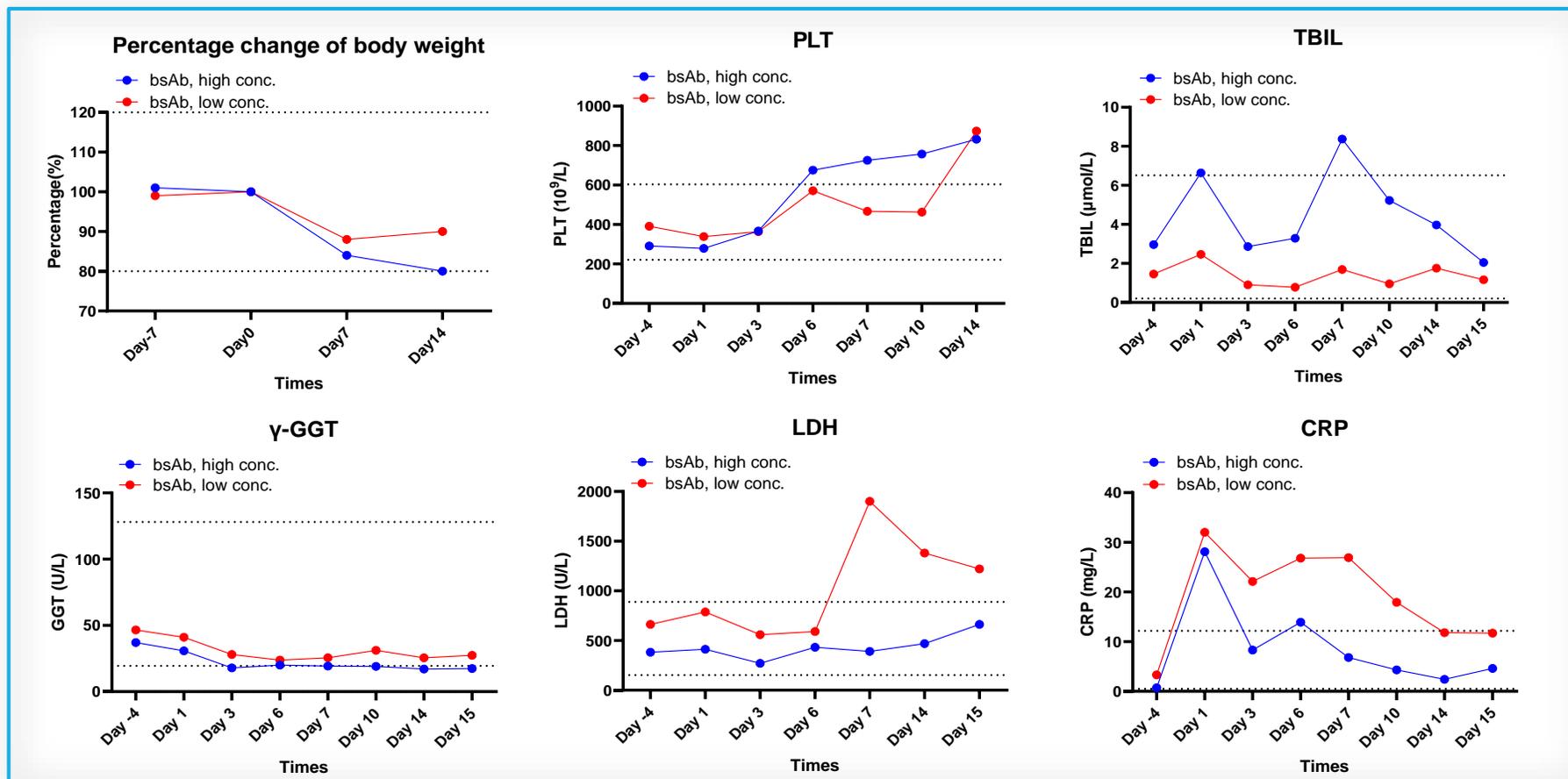
MOA of bsAb (CD3 × Claudin18.2)



■ Study design

Animal species	Test article	Read-outs
Cynomolgus macaque	bsAb	<ul style="list-style-type: none">• Body weight measurement• CBC and Clinical chemistry• PK sampling and analysis• Cytokine and flow cytometric immunophenotyping• Tissue collection and histopathology (HE and IHC staining)

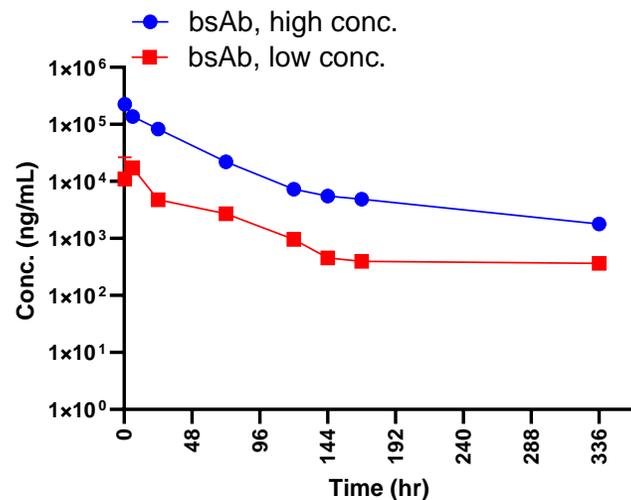
Body weight measurement, CBC and Clinical chemistry



The animals experienced weight loss, abnormal liver function, myocardial damage, and significant inflammation.

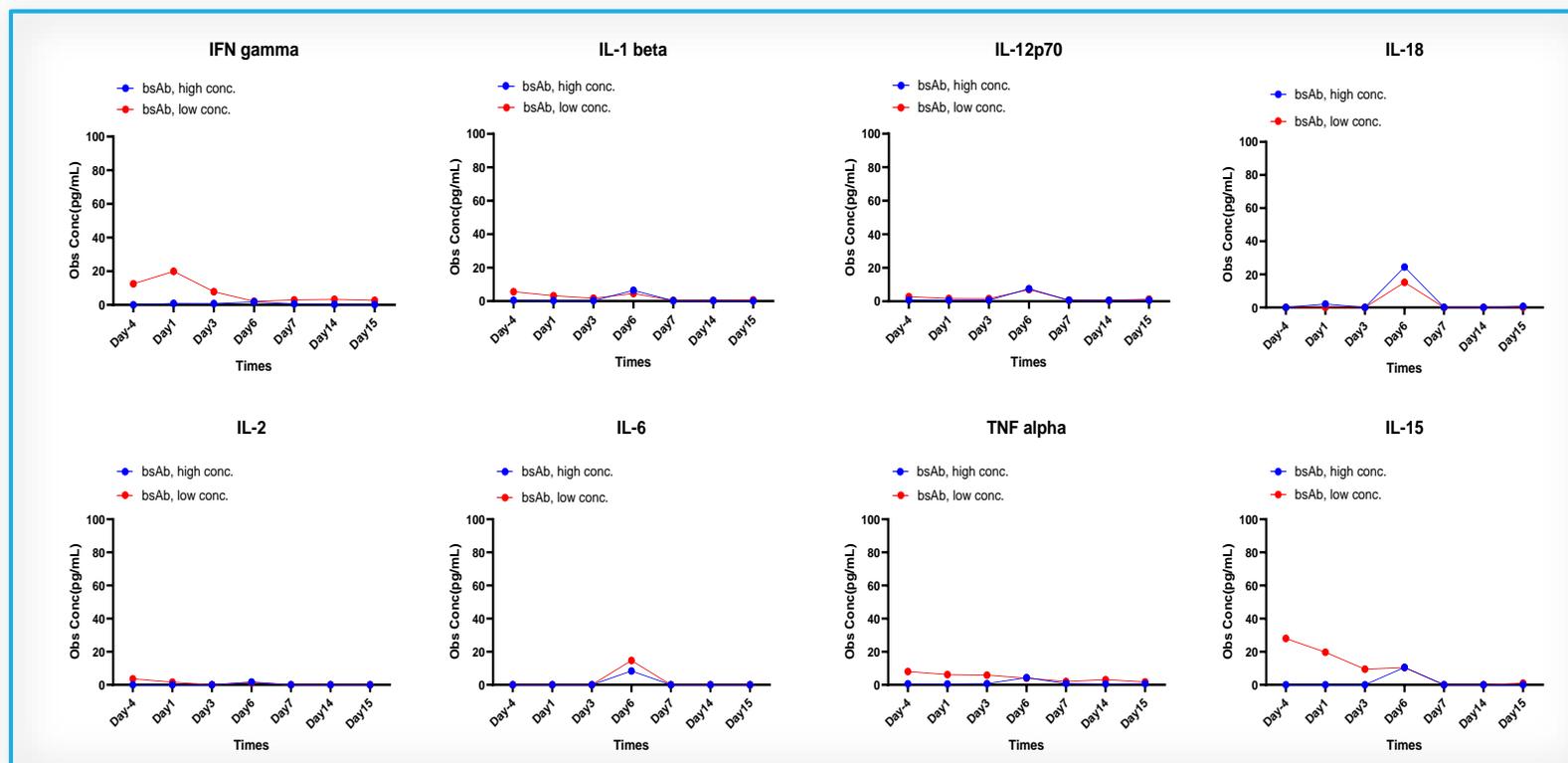
PK and Cytokine results

PK analysis



There was a significant dose effect, the ratio was in line with expectations.

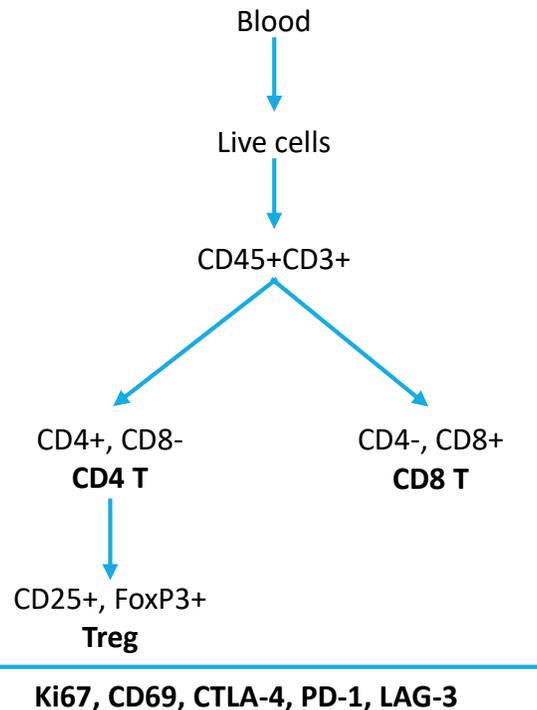
Cytokines assessment: TNF- α , IFN- γ , IL-1 β , IL-6, IL-2, IL-12p70, IL-15, IL-18



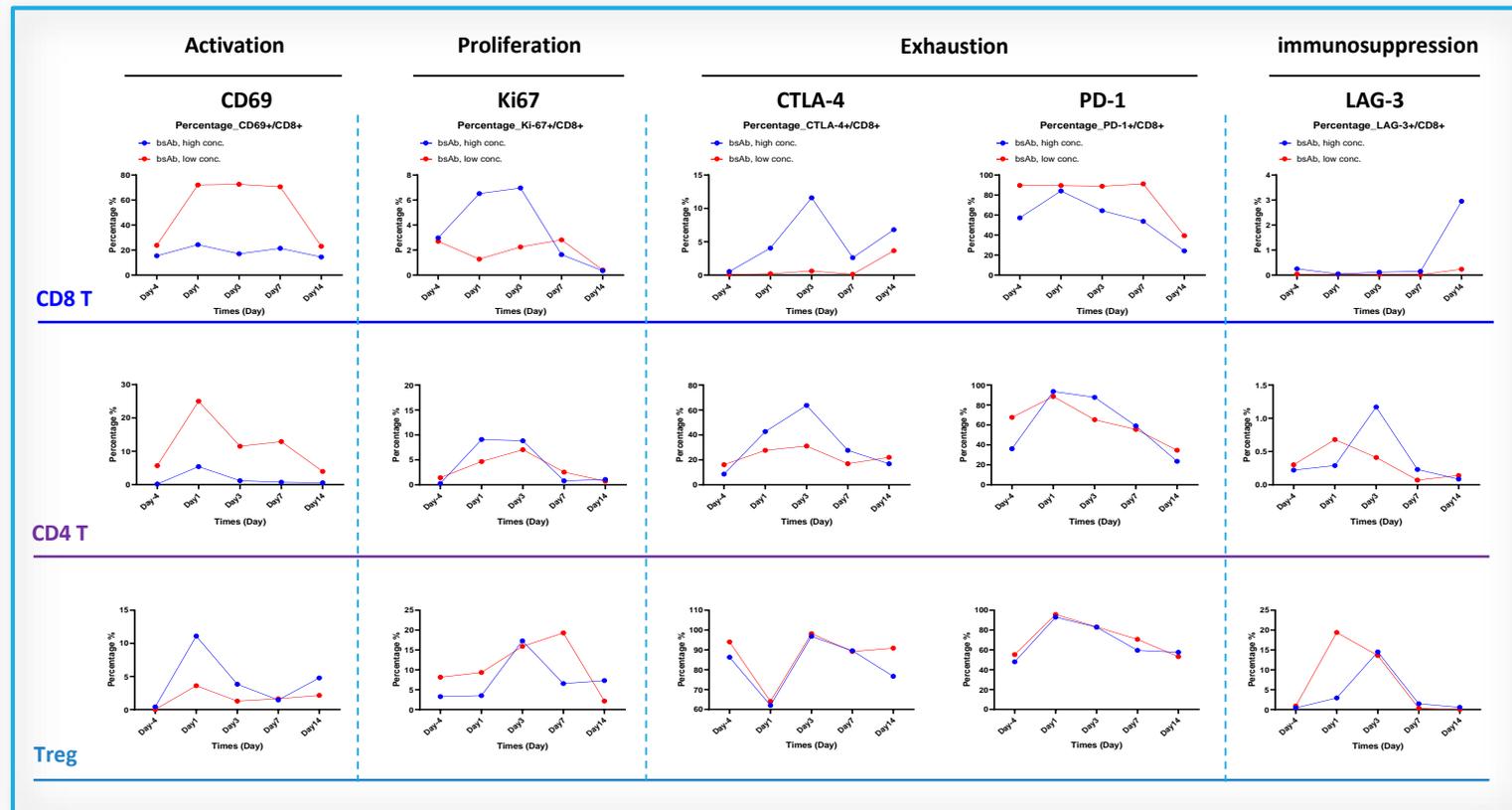
CRS was not detected in peripheral blood.

Flow cytometric immunophenotyping results (Proliferation, activation and exhaustion of T cells)

Panel Design



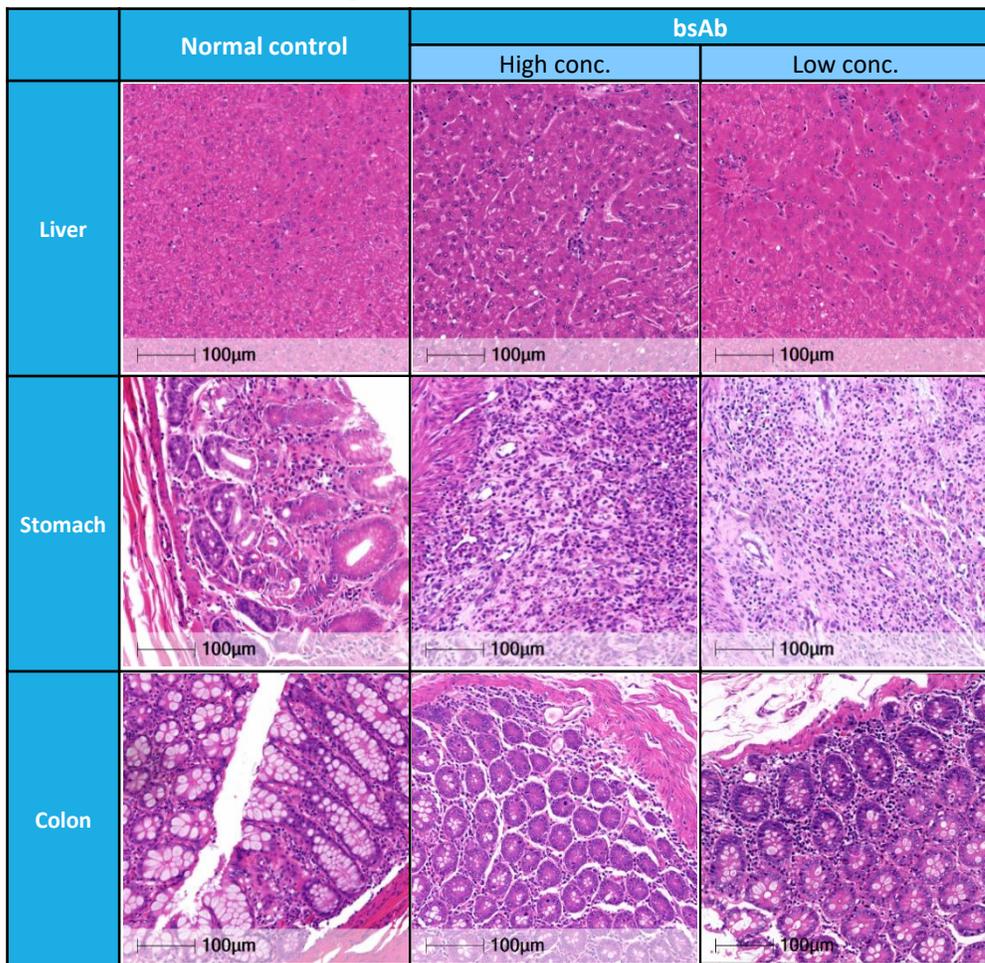
Immunophenotyping



The bsAb accelerated activation, proliferation and exhaustion of T cells.

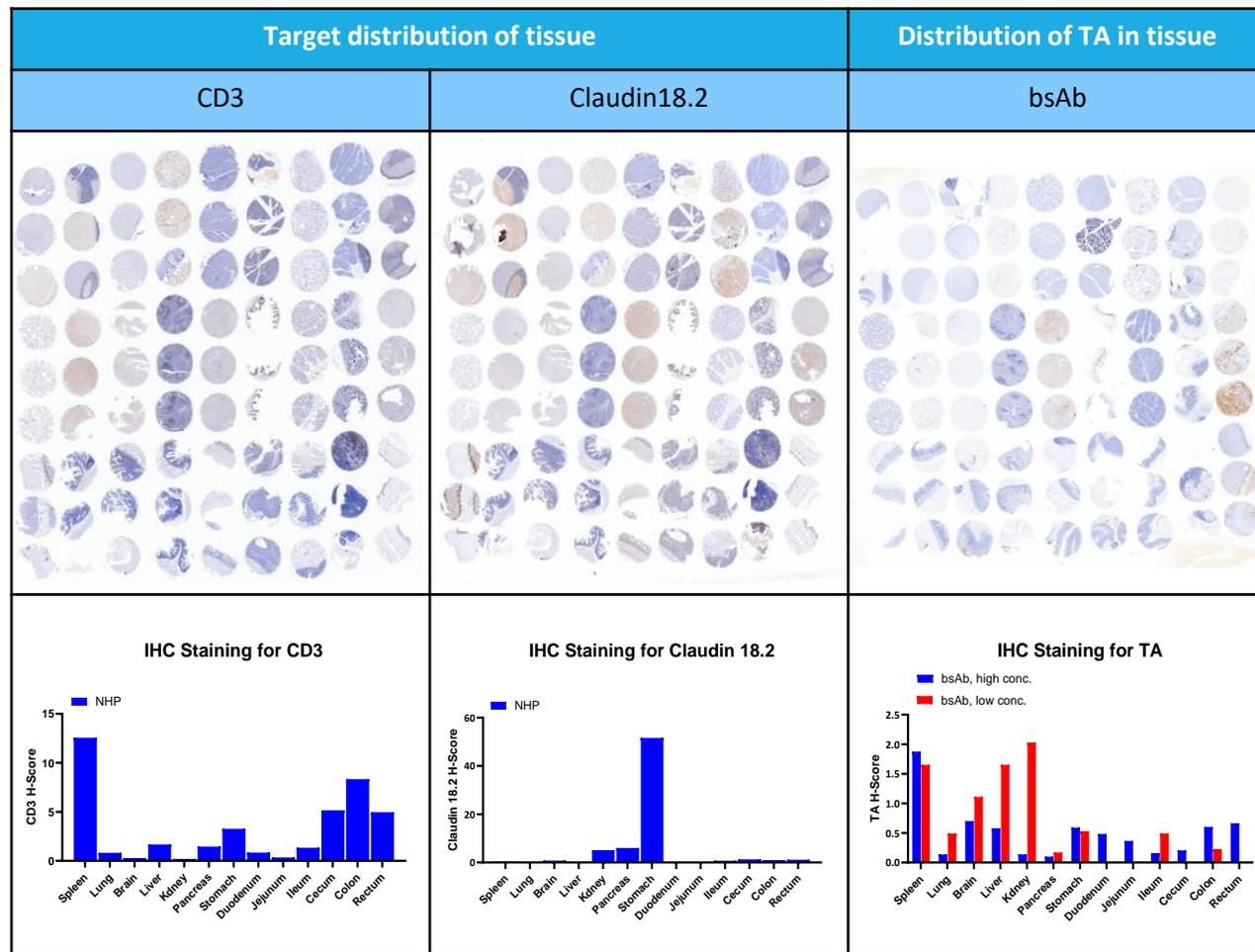
Histopathology results

HE Staining



Abnormal pathological changes in liver and gastrointestinal tract of animals in the administration group may be related to the test article.

IHC Staining





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For questions and requests, please email to Pharmacology-BD-Translation@wuxiapptec.com



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