

# Improved Delivery of ABL301 into Brain Parenchyma of Parkinson's Disease Mouse Brains via Grabody B, ABL Bio's Proprietary BBB Shuttle

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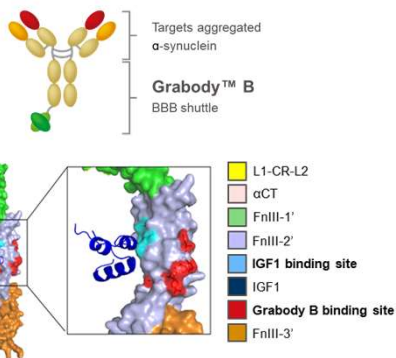
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## Objectives

- ❖ ABL301 is a bispecific antibody composed of an **anti- $\alpha$ -synuclein antibody (M30103) with Grabody B, an anti-IGF1R** as the ABL Bio's proprietary BBB technology.
- ❖ Previous study demonstrated improved efficacy of ABL301 than M30103 in a mouse model of Parkinson's disease. The current study aims to identify 1) temporal and spatial movement of ABL301 out of brain vessel in a Parkinson's disease animal model, 2) its PK profile, and 3) expression profile of IGF1R in postmortem brains.

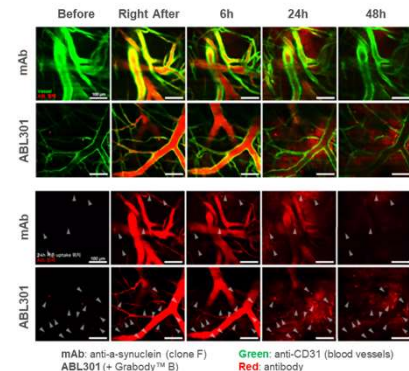
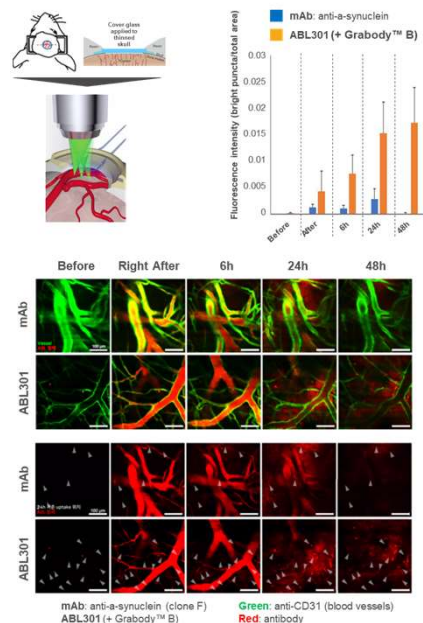
## Results

### Binding site to the protein & species cross-reactivity of Grabody B

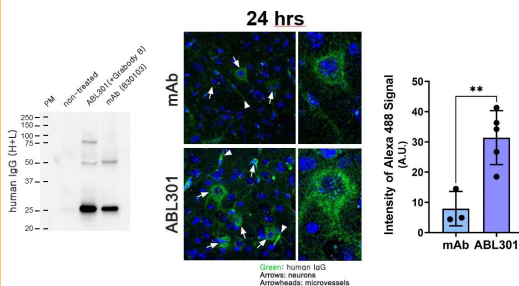


Methods	IGF1R species	Grabody B
SPR (Biacore)	Human	$K_D$ (M): $5.43 \times 10^{-8}$
	Mouse	$K_D$ (M): $0.87 \times 10^{-8}$
	Rat	$K_D$ (M): $6.44 \times 10^{-8}$
	Cyno	$K_D$ (M): $3.20 \times 10^{-8}$

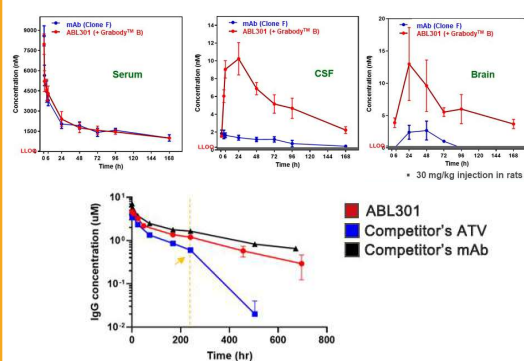
### Effective penetration and retention in mThy1 PD mouse brains



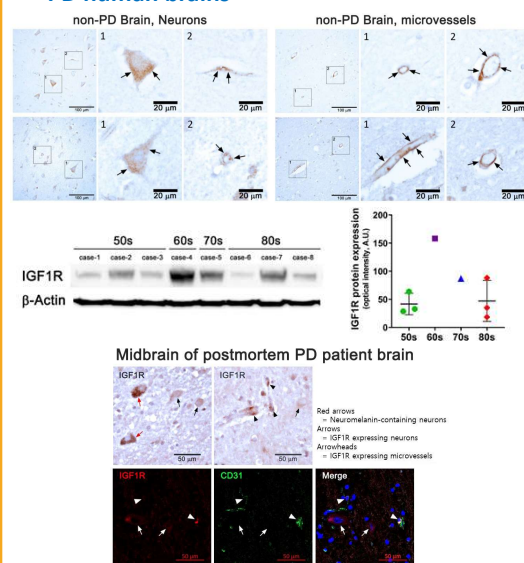
### Detection & biodistribution of human IgG in parenchyma of mThy1 PD mouse brains



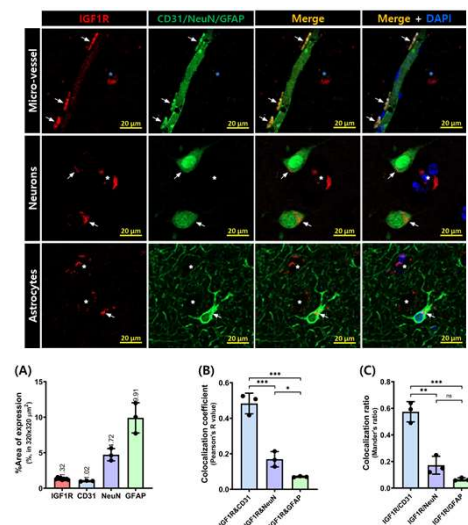
### PK improvement in rats & superior NHP serum PK of Grabody B



### IGF1R expression in postmortem non-PD & PD human brains



### Colocalization of IGF1R with CD31/NeuN/ GFAP in postmortem human brains



## Conclusions

- ❖ ABL301 is localized into brain parenchyma, possibly to its target, aggregated  $\alpha$ -synuclein with higher degree than M30103.
- ❖ Its superior serum PK comparable to mAb might have contributed to its sustained BBB penetration over time.
- ❖ IGF1R expression in capillary and endothelial cells in postmortem brains partially validates Grabody B's usage as a BBB shuttle in clinical studies.