

Characterization and Development of JADE301, a Half-Life Extended Anti-IFN-β Monoclonal Antibody for Treatment of Dermatomyositis



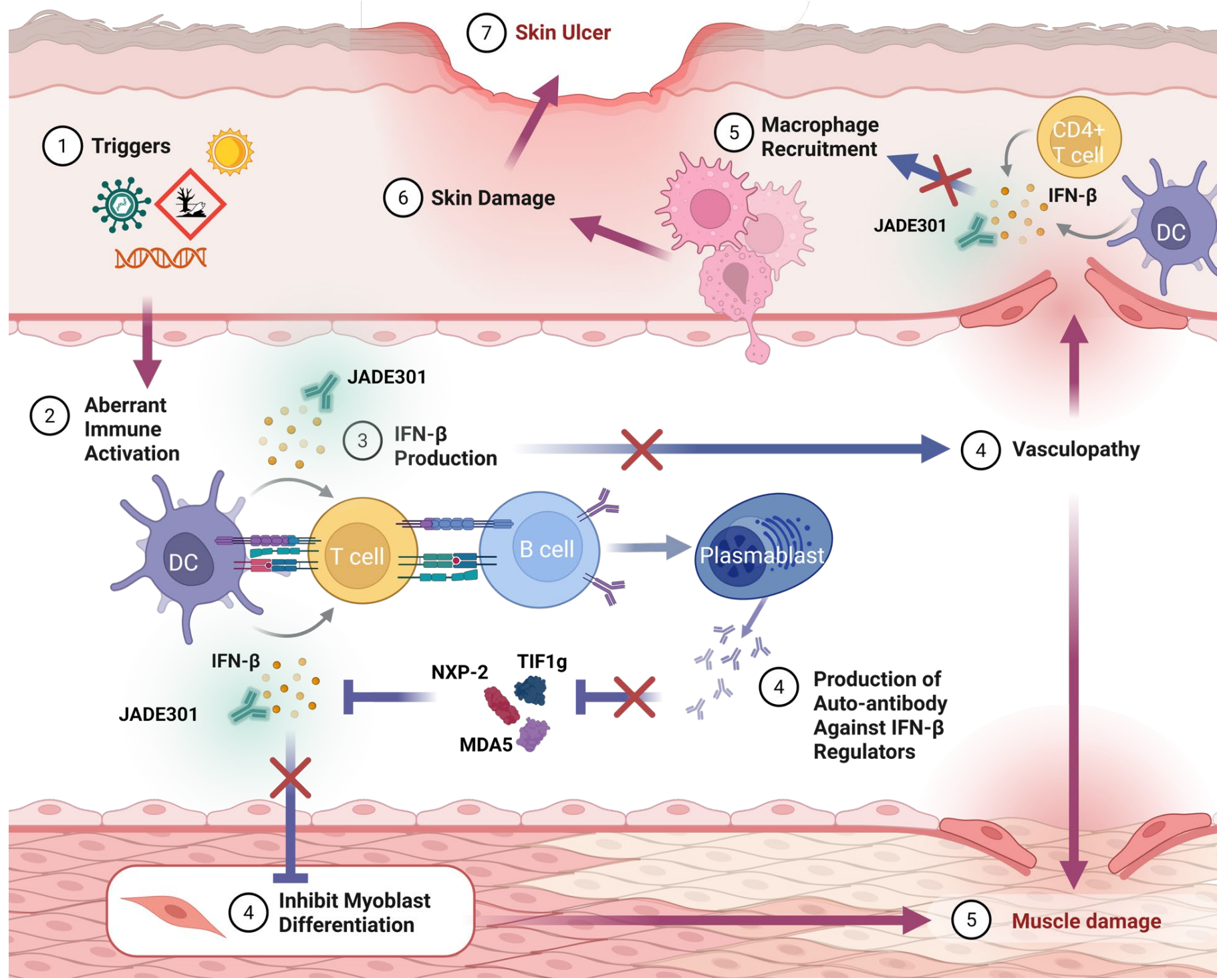
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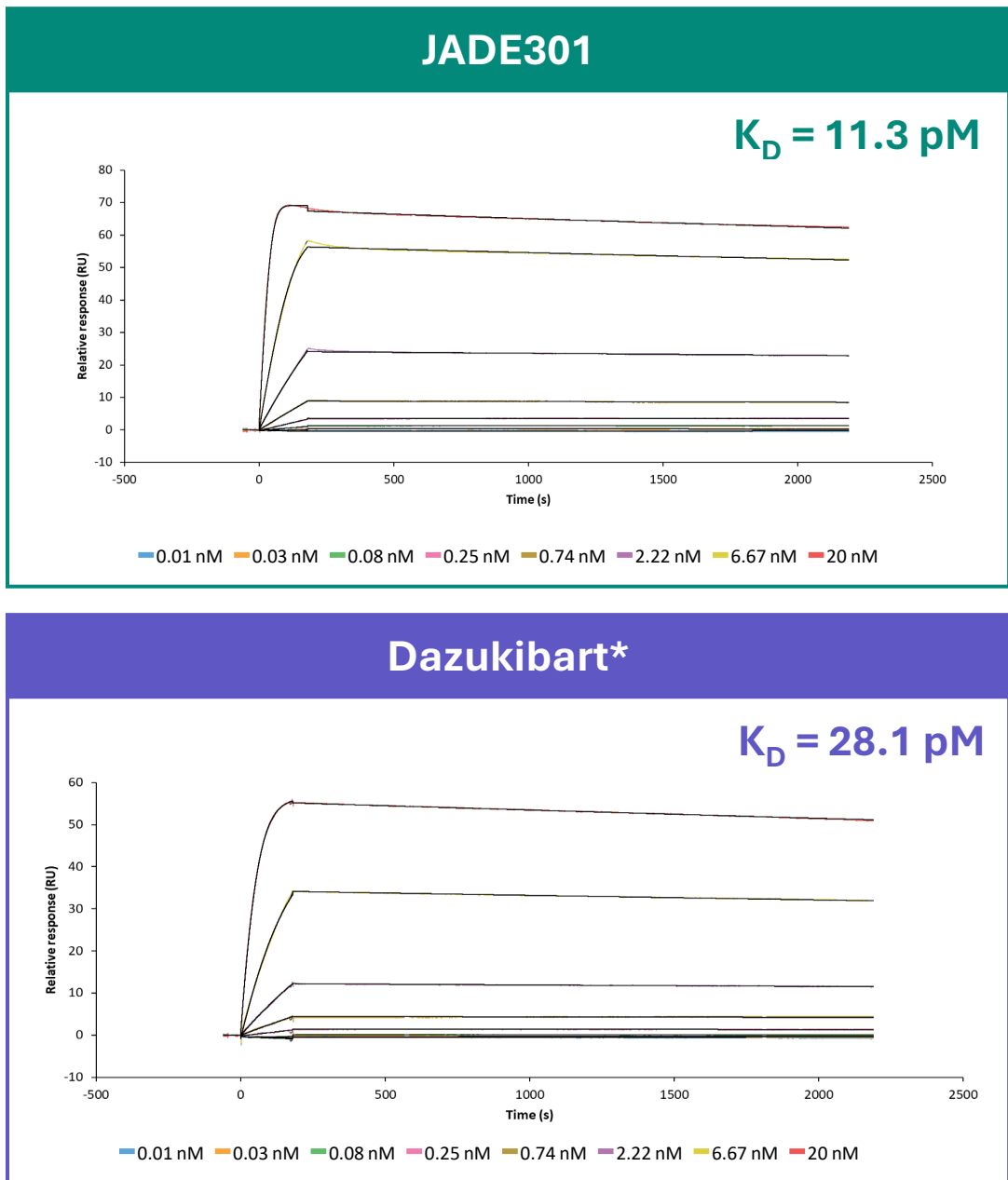
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Background

- Dermatomyositis (DM) is a chronic autoimmune myopathy characterized by a strong Type I interferon (IFN) gene signature in blood, skin, and muscle, which correlates with disease activity and severity (*Baecler EC, Arthritis Res Ther. 2011*).
- Aberrant IFN-β signaling is a key pathogenic driver of both cutaneous and muscular inflammation in DM and specific neutralization of IFN-β has demonstrated promising clinical efficacy in DM patients (*Werth VP, The Lancet 2024*).
- JADE301 is a novel, fully human IgG1 monoclonal antibody that specifically and potently neutralizes IFN-β and blocks its interaction with interferon-α/β receptor (IFNAR).
- JADE301 was selected for high affinity and potency and designed with a YTE modification for extended half-life in humans, potentially enabling convenient, infrequent, subcutaneous dosing in DM patients.

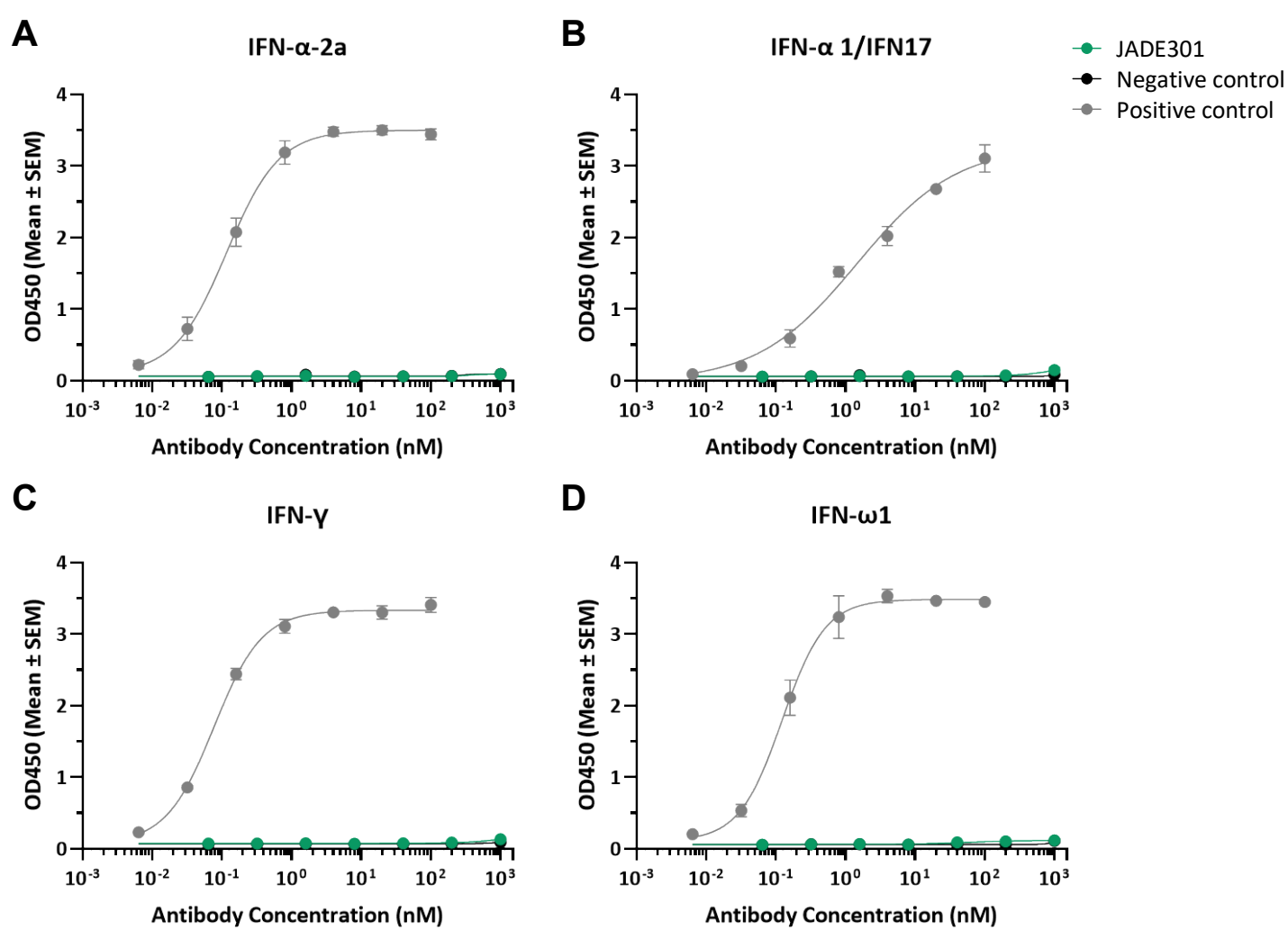


JADE301 Binds IFN-β with High Affinity and Selectivity



SPR binding of JADE301 or dazukibart* to recombinant human IFN-β

*dazukibart generated internally from publicly available sequence.



IFN-family proteins were coated on ELISA plates and incubated with serial dilutions of JADE301 (green) or protein-specific positive control antibodies (gray). Binding was detected by HRP-conjugated secondary antibody and absorbance at 450 nm. JADE301 showed no detectable binding to IFN-α - 2a (A), IFN-α 1/ IFN17 (B), IFN-γ (C) or IFN-ω1 (D); supporting selective binding specificity for IFN-β.

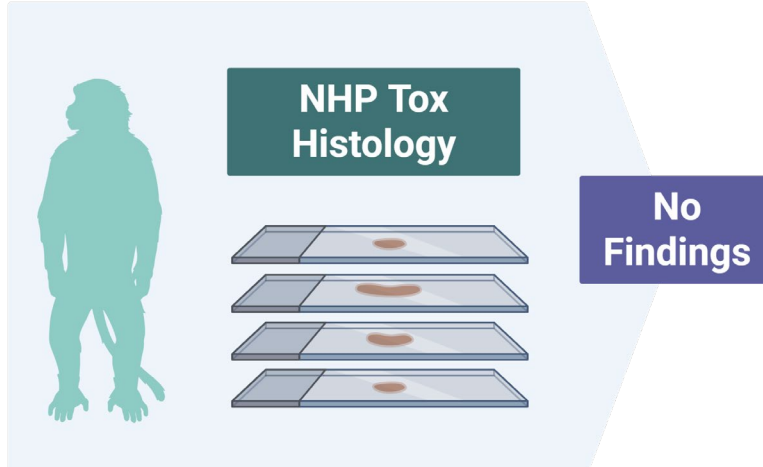
Predicted Favorable SC Bioavailability in Human

Method#	Equations	NHP CL	Isoelectric Point (pI)	Predicted Human SC Bioavailability
Model using observed NHP CL and sequence-based pI	$F = 1.08 - 0.0405 \times \text{pI} - 0.0156 \times \text{CL}_{\text{NHP}}$	2.2 mL/day/kg	7.4 (theoretical)	0.75
Model using observed NHP CL and 3D pI of Fv region	$F = 0.981 - 0.0298 \times \text{3D_pI} - 0.0146 \times \text{CL}_{\text{NHP}}$			0.73

Predicted JADE301 SC bioavailability > 73%
Reported dazukibart human SC bioavailability: ~43 to 44%*

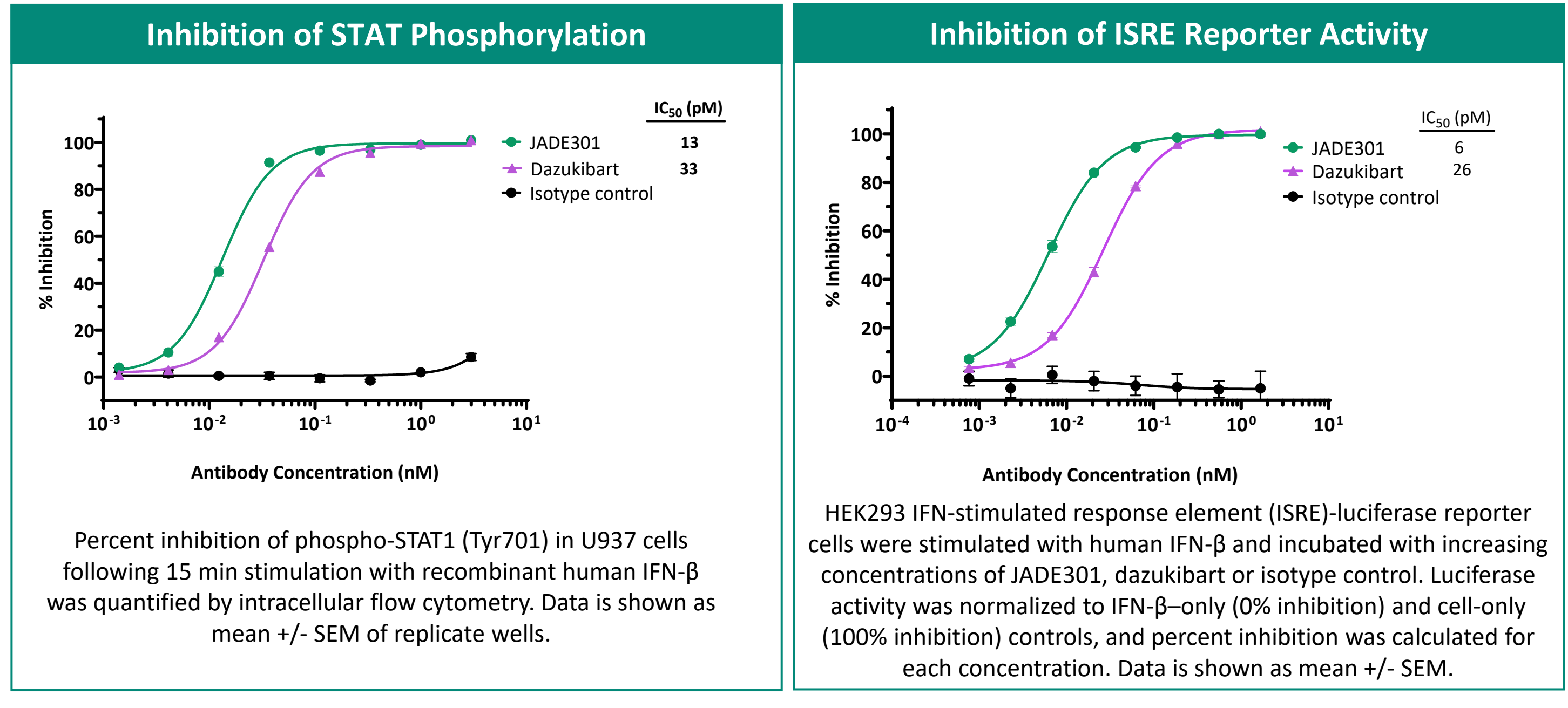
^{##} Zou P. Predicting Human Bioavailability of Subcutaneously Administered Monoclonal Antibodies Using Non-human Primate Linear Clearance and Antibody Isoelectric Point. *AAPS Journal*. 2023
^{*}Neelakantan S. Safety, Tolerability, and Pharmacokinetics of PF-06823859, an Anti-Interferon β Monoclonal Antibody: A Randomized, Phase I, Single- and Multiple-Ascending-Dose Study. *Clinical Pharmacology in Drug Development*. 2021.

JADE301 is Well-Tolerated in Non-Human Primates

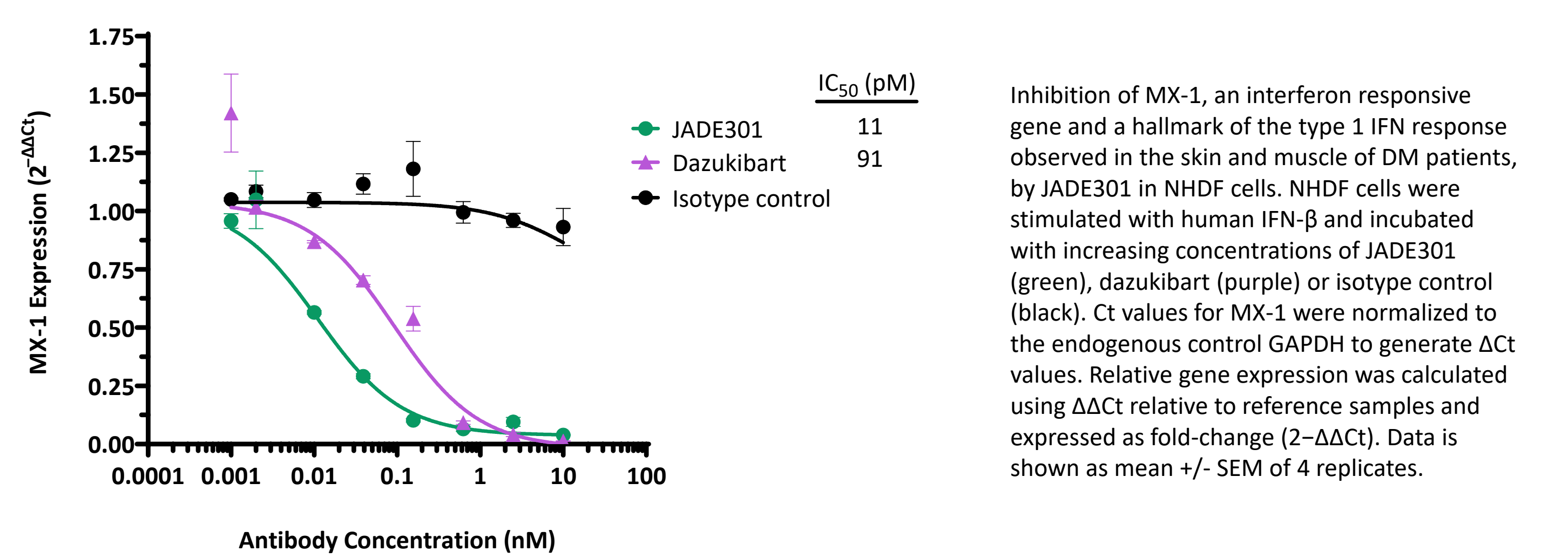


- NHPs were dosed in a 29-day GLP Toxicology Study with JADE301 (SC) at 0, 50, 100, or 200 mg/kg Q2W. At the end of the dosing phase tissues were collected for histology.
- JADE301 was well tolerated up to 200 mg/kg, with no treatment-related adverse clinical observations or meaningful adverse events on clinical chemistry, hematology, histology or other standard safety assessments.
- Muscle distribution of JADE301 was ~1-4% of serum concentrations, consistent with a typical mAb (*Shah, D.K., & Betts, A.M. mAbs 2013*) and indicating no apparent effect of YTE modification on muscle distribution.

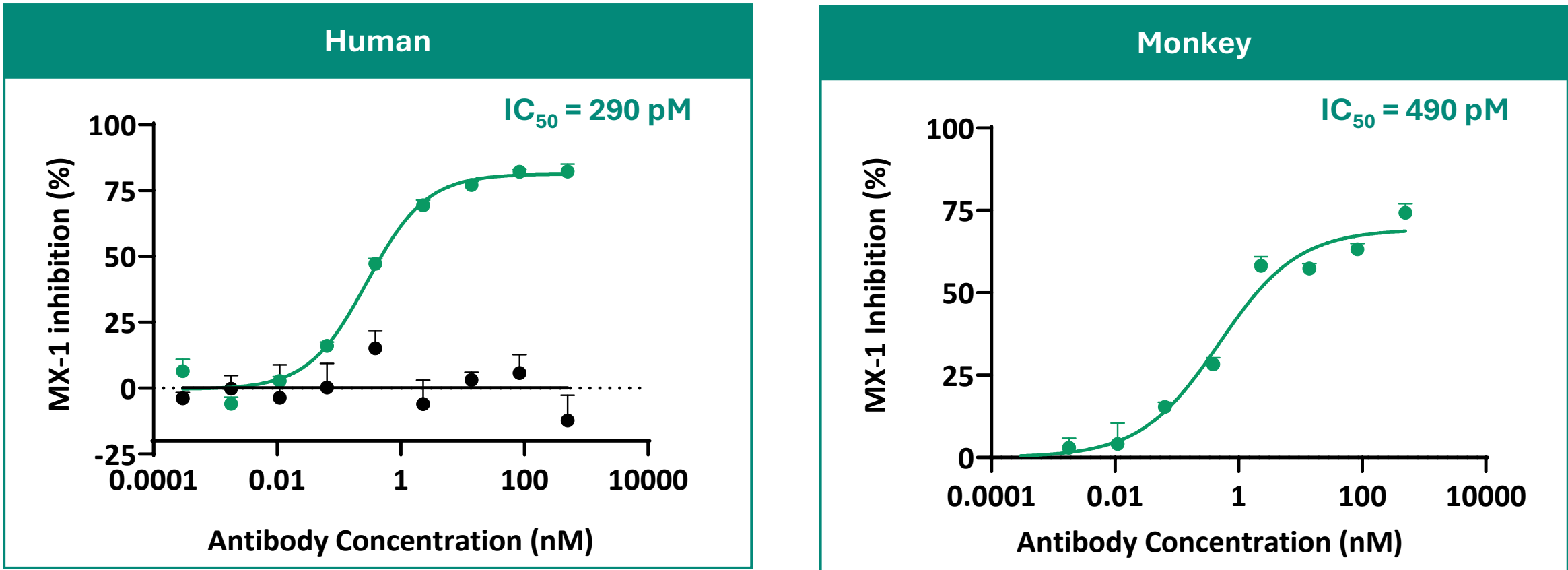
JADE301 Blocks IFN-β Signaling Through IFNAR



JADE301 Potently Suppresses Expression of MX-1 in Human Dermal Fibroblasts (NHDF)

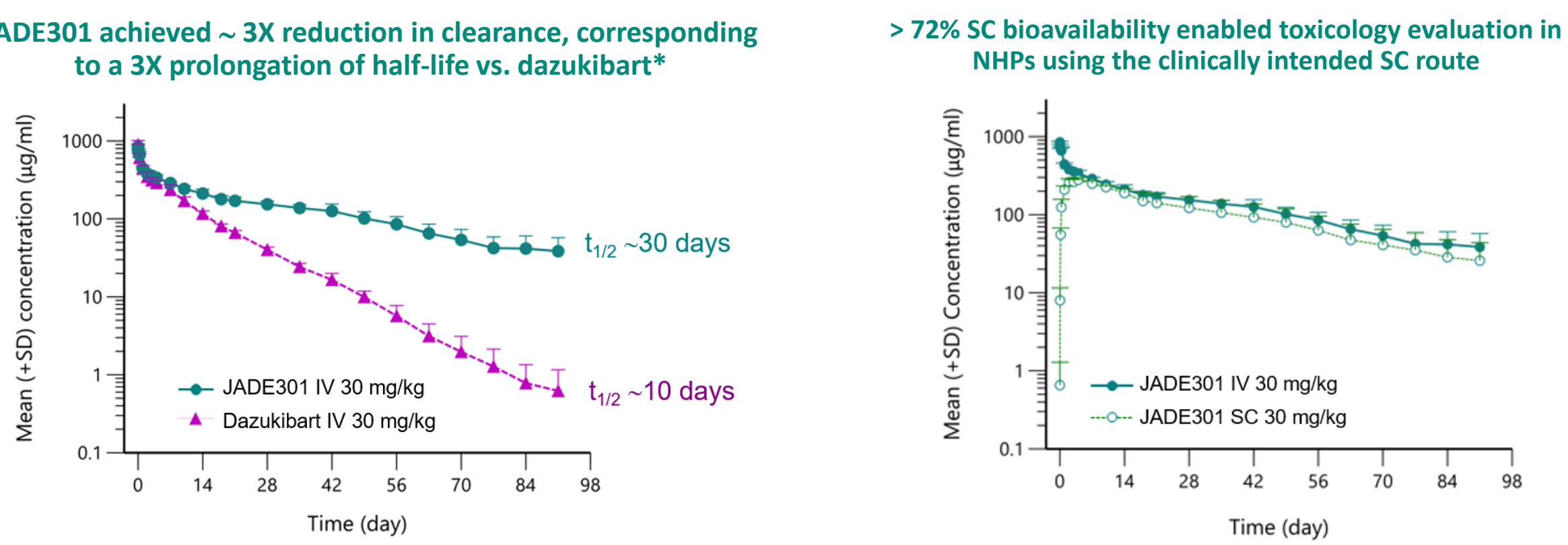


JADE301 Potently Suppresses Expression of MX-1 in Human and Monkey PBMC



Human or cynomolgus monkey PBMC were stimulated with IFN-β and incubated with increasing concentrations of JADE301 (green) or isotype control (black). Gene expression was analyzed using the comparative CT (ΔΔCt) method and converted to percent inhibition of MX-1 induction by normalizing against the IFN-β-only positive control. Human data is representative of 3 experiments with 2 different donors and monkey data is representative of 2 donors. Data is shown as mean +/- SEM of duplicates.

JADE301 Exhibits an Extended Half-Life in NHP



Parameter (units)	Dazukibart* (30 mg/kg IV)	JADE301 (30 mg/kg IV)	JADE301 (30 mg/kg SC)
Half-life t _{1/2} (day)	10 (1.8)	30 (7.5)	25 (8.3)
CL or CL/F (mL/day/kg)	5.9 (0.4)	2.2 (0.5)	3.3 (1.4)
V _r or V _d /F (mL/kg)	73 (12)	92 (7.6)	105 (4.6)

PK parameters presented as mean (SD) from n = 3-4 monkeys/group. Confirmed ADA positive samples and impacted PK parameters excluded.

Conclusions

- JADE301 is a novel anti-IFN-β neutralizing antibody with high affinity and extended pharmacokinetic half-life that potently inhibits signaling through IFNAR and subsequent expression of IFN-stimulated genes (ISGs), consistent with the potential for robust suppression of Type I IFN signaling pathways that drive DM pathogenesis.
- The favorable tolerability profile observed in NHPs, together with extended half-life and potent IFN-β neutralization, supports clinical evaluation of JADE301 as a targeted therapeutic approach with potentially reduced treatment burden for patients with DM.
- The characterization of the pharmacological profile of JADE301, combined with NHP PK and tissue distribution, provides a translational framework for dose selection in DM patients to ensure robust IFN-β neutralization locally at sites of active disease in the skin and muscle.