

P4-02 #3254 NIDB-3101, A NOVEL BIPARATOPIC ANTI-TAU ANTIBODY: CHARACTERIZATION OF ITS PHARMACOKINETICS, PHARMACODYNAMICS AND TOLERABILITY

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Background

NIDB-3101 is a third-generation anti-tau antibody (Ab) developed to increase the likelihood of clinical efficacy and safety in Alzheimer's Disease (AD). It incorporates three key design features:

- a biparatopic Ab format targeting two different epitopes - R4 and C-terminal (Ct) regions – conferring high apparent affinity.
- half-life extension mutations enabling less-frequent dosing in patients while increasing exposure for a given dose.
- mutations abrogating Fc-mediated effector functions to reduce the risk of neuroinflammation, which is particularly relevant when combining an anti-tau with an anti-A β Ab.

Using human AD brain material, NIDB-3101 was shown to capture a broader range of tau species than other anti-tau Abs, even in the presence of tau truncation or post-translational modifications. The *in vitro* characterization data for NIDB-3101 have been reported previously (1).

NIDB-3101, a native fully human biparatopic anti-tau $\kappa\lambda$ body

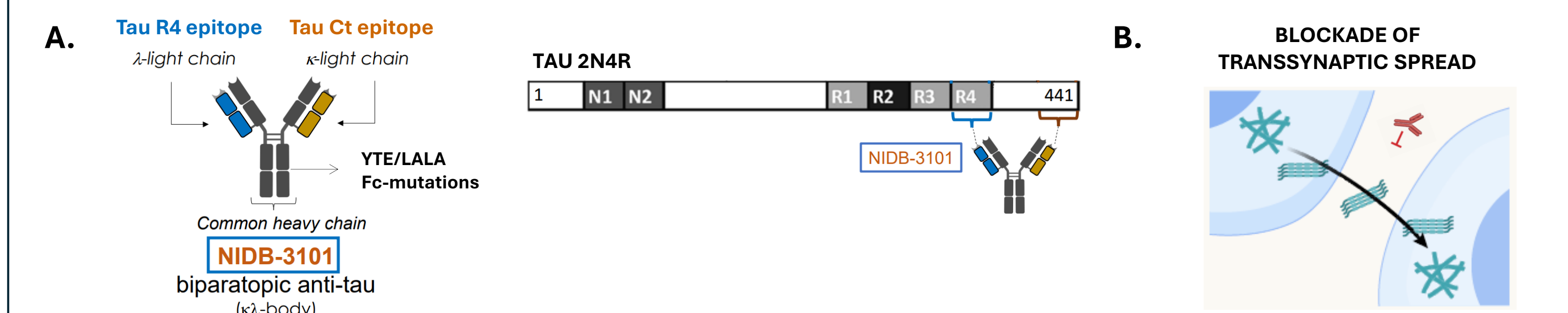
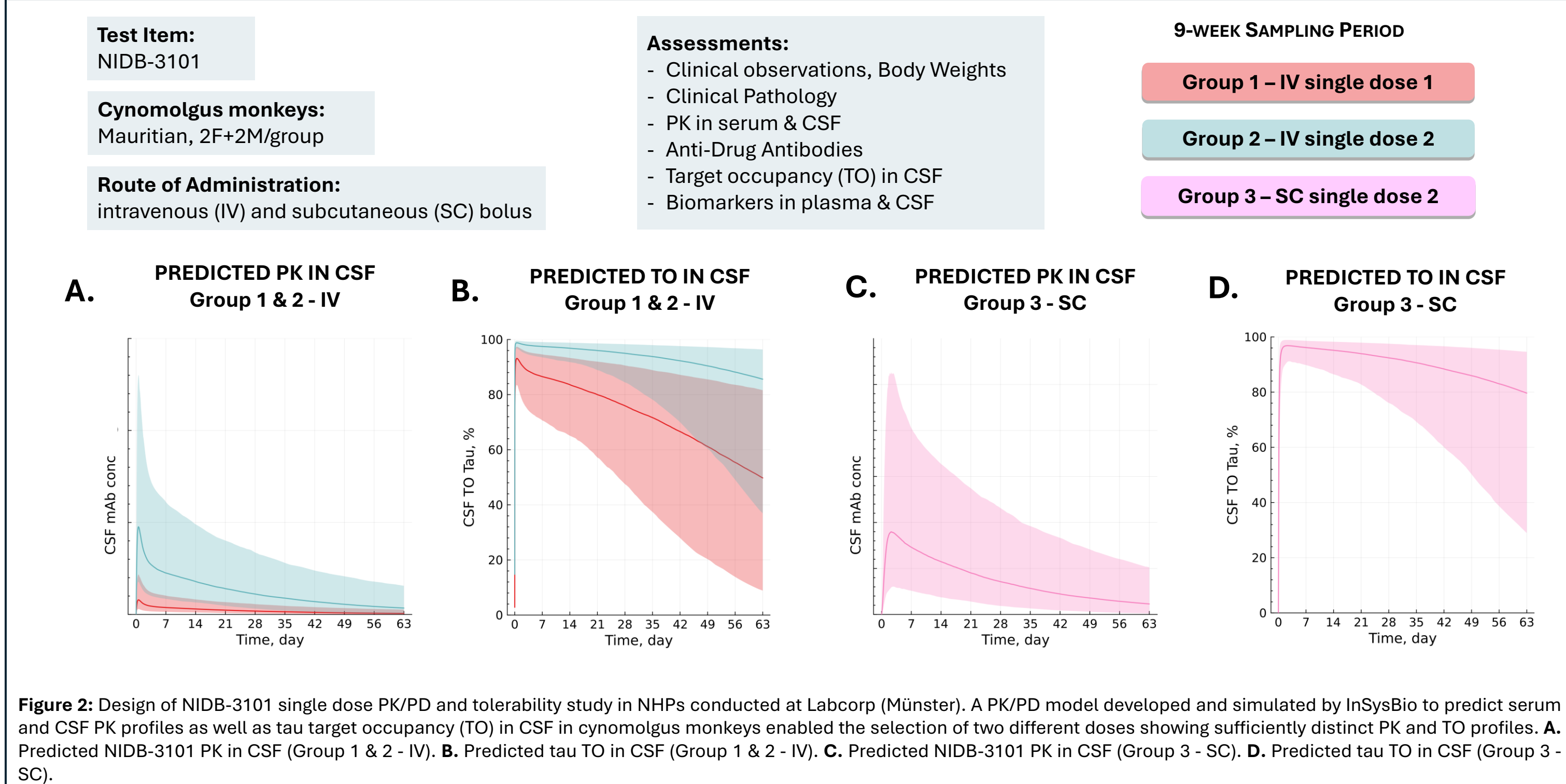


Figure 1: A. Schematic structure of NIDB-3101, pairing anti-tau arms recognizing the fourth domain of the microtubule binding region and the Ct domain of tau into a fully human and native $\kappa\lambda$ body format. B. Schematic of NIDB-3101 mode of action (adapted from 2).

NIDB-3101 single dose PK/PD & tolerability study in NHP



NIDB-3101 was well tolerated

- No NIDB-3101-related clinical observations following dosing
- No drug-related body weight change during the study
- 48 h post-dose:
 - Hematology: no drug-related changes
 - Clinical chemistry: no drug-related changes
- End of treatment period:
 - Macroscopic observations: no drug-related changes
 - Microscopic observations: under evaluation

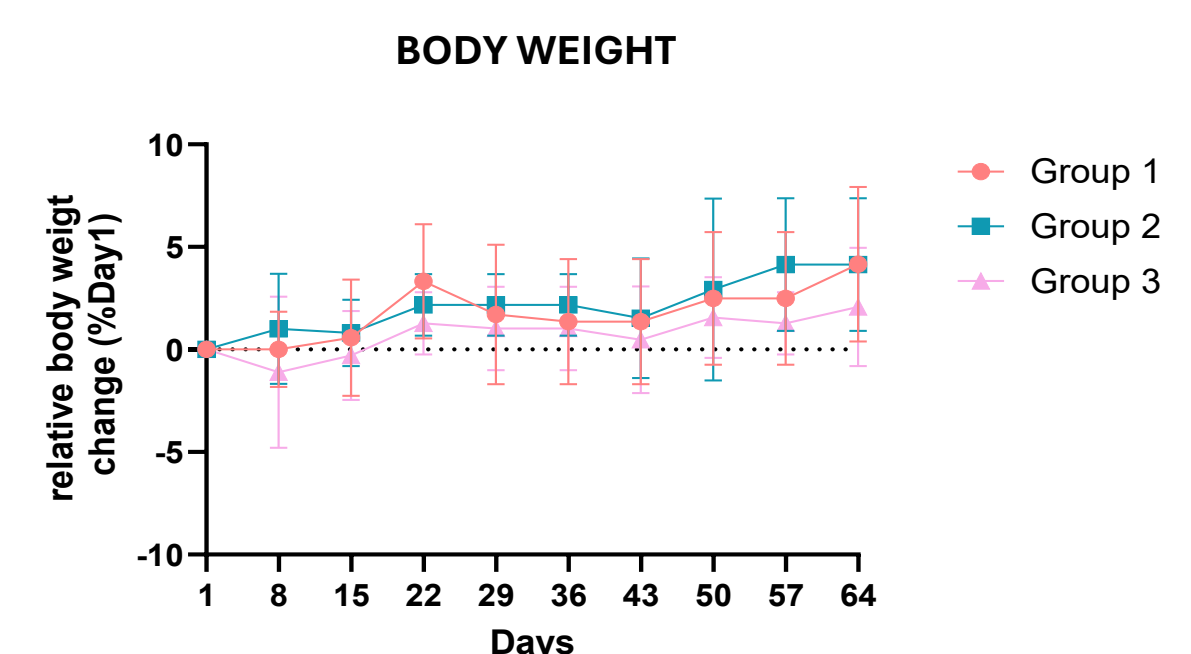
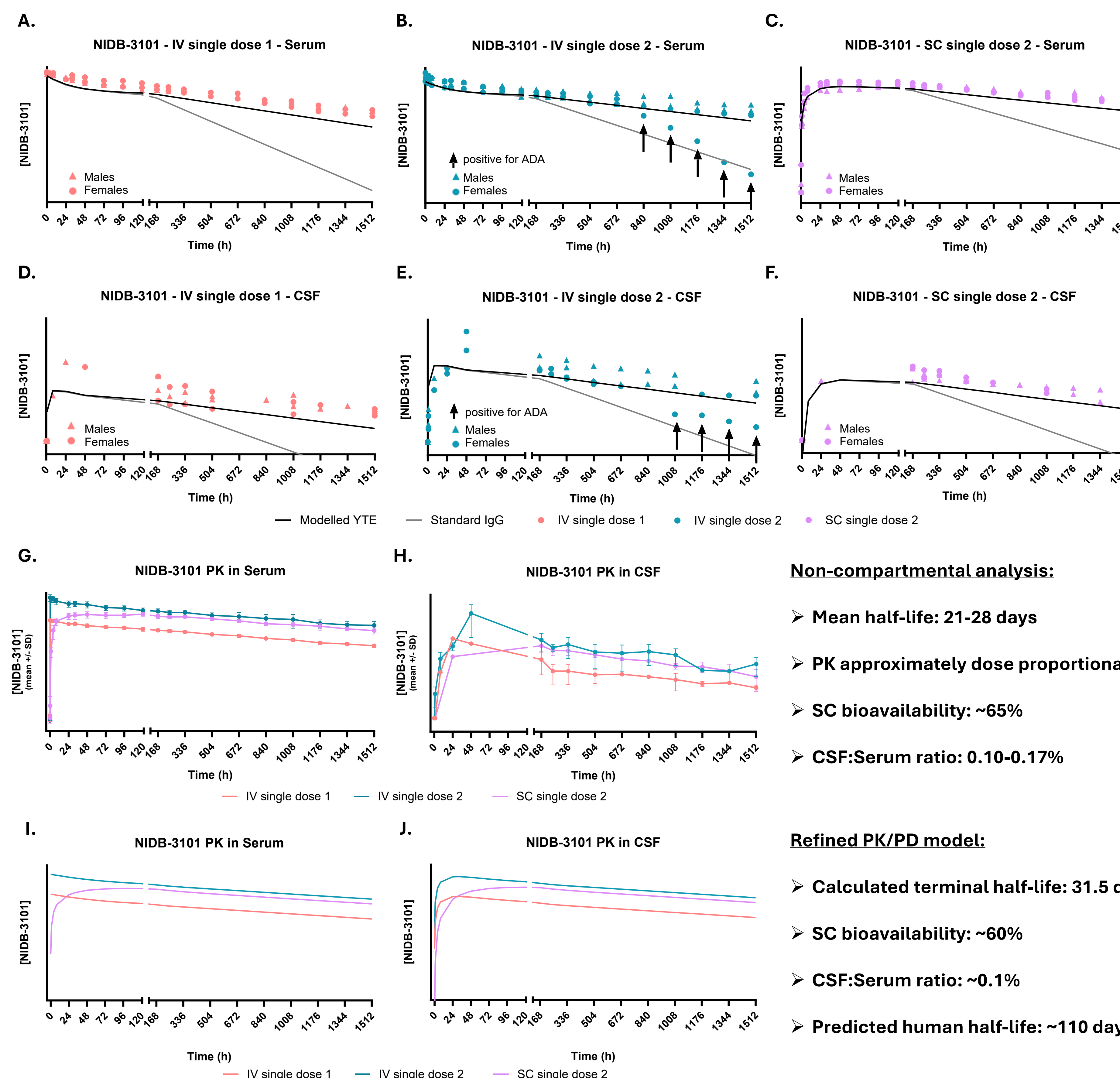


Figure 3: Summary of clinical and physical examinations (including mortality, clinical observations, body weights, and food intake monitoring) as well as clinical pathology (standard hematology and clinical chemistry parameters, 48 h post-dose) and post-mortem examinations (comprising gross pathology and histopathology of selected organs conducted at the end of the study).

YTE mutation extends half-life and enhances serum and CSF exposure of NIDB-3101



Conclusions

- Favourable Safety Profile:** NIDB-3101 was well tolerated in NHPs following single IV and SC administrations at all tested doses.
- Superior PK Performance:** NIDB-3101 achieved extended serum and – critically – CSF half-lives in NHPs (31.5 days) compared to standard IgG (7.5 days).
- Clinical Translation:** Predicted human half-life of ~110 days supports a significantly lower dosing frequency and reduced total dose compared to standard antibodies.
- Next steps:** NIDB-3101 is currently progressing through GLP toxicology studies to enable First-in-Human trials. CSF target occupancy data will be presented at CTAD 2026.
- Conclusion:** These first *in vivo* data highlight the clear therapeutic advantages of NIDB-3101 as a third-generation biparatopic anti-tau antibody over previous generations.