

Model-Based Assessment of Clinical Responses to APRIL Blockade Informing Development of the anti-APRIL mAb JADE101 in IgAN

B. Gufford, T. DeVries, V. Tong, S. Lewis, L. Li, E. Filbert, and A. King¹

¹Jade Biosciences, San Francisco, United States and Vancouver, Canada

Background

- IgA nephropathy (IgAN) is a progressive autoimmune kidney disease characterized by mesangial deposition of immune complexes containing IgA and Gd-IgA1.
- Neutralizing A proliferation-inducing ligand (APRIL) is potentially disease-modifying in IgAN by depleting IgA and Gd-IgA1, reducing proteinuria, and ultimately stabilizing eGFR without impacting B-cell development and maturation.
- JADE101 is a novel APRIL-neutralizing human IgG1 monoclonal antibody (mAb) designed with ultra-high affinity and extended half-life to optimize clinical activity and enable infrequent subcutaneous (SC) dosing.
- Biomarker responses to APRIL inhibition can be integrated across studies and molecules using pharmacokinetic (PK) and pharmacodynamic (PD) models to predict anticipated clinical responses in IgAN, informing development of APRIL-targeted therapies.

Methods

- Population-based clinical PKPD models were used to integrate data from the JADE101 development program with publicly available clinical data in healthy volunteers and patients with IgAN, including studies of anti-APRIL mAbs and dual APRIL/BAFF inhibitors.
- Model-based simulations were used to predict PD outcomes supporting dose regimen selection targeting biomarker responses relevant to IgAN drug development. Predicted outcomes were compared to observed data to assess robustness of the modeling framework.

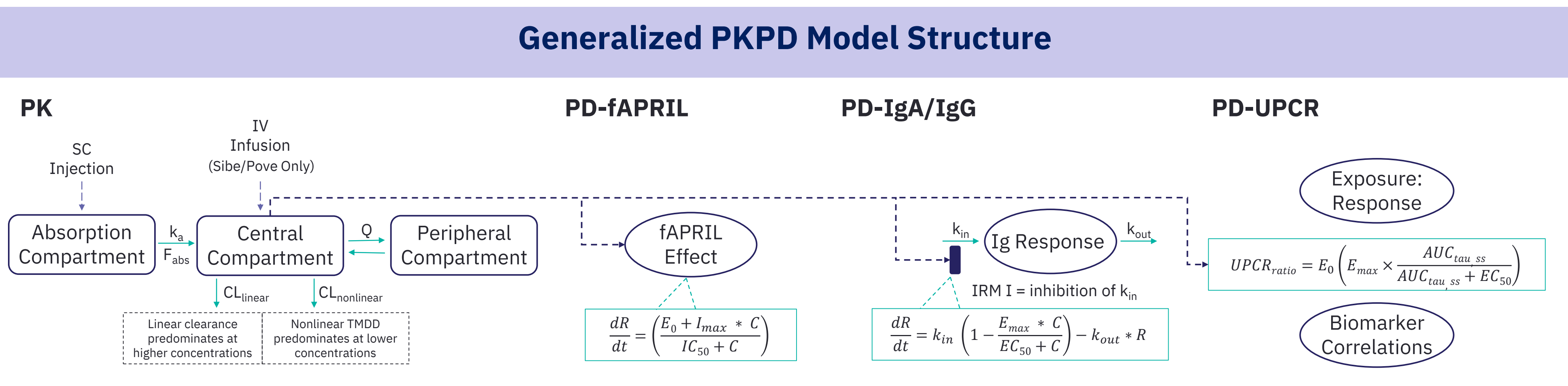


Figure 1. Generalized population-based PKPD model structures supporting integrated modeling and simulation-based assessment of key pharmacodynamic and clinical responses in a representative virtual IgAN patient population. Models leverage the same generalized structure with appropriate molecule-specific inputs included as available or estimated from available data across molecules and participant populations. PK exposure serves as the driving input function for downstream PD effects including fAPRIL neutralization (direct effect), immunoglobulin reduction (indirect effect), and UPCR lowering (simple E_{max} exposure:response).

Conclusions

- An integrated modeling approach leveraging available data from the JADE101 development program in conjunction with data available in the public domain provides a robust description of observed and anticipated pharmacodynamic biomarker responses in a representative IgAN patient population.
- Integration of rich biomarker datasets across molecules/clinical trial phases provides a quantitative framework to predict potential clinical responses to APRIL-blockade.
- The PK-IgA and PK-IgG model predictions suggests that JADE101 can potentially lower IgA without additional risk of hypogammaglobulinemia.
- The evaluated PK-IgA-UPCR relationships indicate that consistently maximizing early IgA reductions could optimize later UPCR responses across a representative IgAN population.
- The model-informed drug development approach underpins JADE101 development as a potentially disease-modifying therapy in IgAN with potential for convenient SC dosing as infrequently as every 12 weeks.

Results

Key Simulated and Observed IgAN Population Characteristics

Integrated Population-based models can be leveraged to generate a representative virtual IgAN patient population for assessment of targeted biomarker responses

Baseline Characteristic Mean [range]	Observed IgAN Population (N=367)	Simulated IgAN Population (N=500)
Age (years)	41 [18 - 75]	42.6 [18.2 - 73.9]
Body weight (kg)	74.0 [40.2 - 238]	77.2 [42.4 - 165]
fAPRIL (pg/mL)	3430 [228 - 49900]	3790 [440 - 38100]
IgA (mg/dL)	315 (150)	307 [117 - 788]
IgG (mg/dL)	1110 (129)	1110 [662 - 2220]

Table 1. Observed IgAN population characteristics obtained from published data (Voyxact, 2025; Mathur, 2024). Observed IgAN population IgA and IgG reflect the pooled mean (SD) baseline across all Ph2 dose levels and placebo. Simulated IgAN population characteristics obtained from representative integrated population-based model (N=500).

Model Predicted vs. Observed IgA Reductions

Integrated PK-IgA response models accurately reproduce published IgA model simulations and capture observed clinical IgA profiles

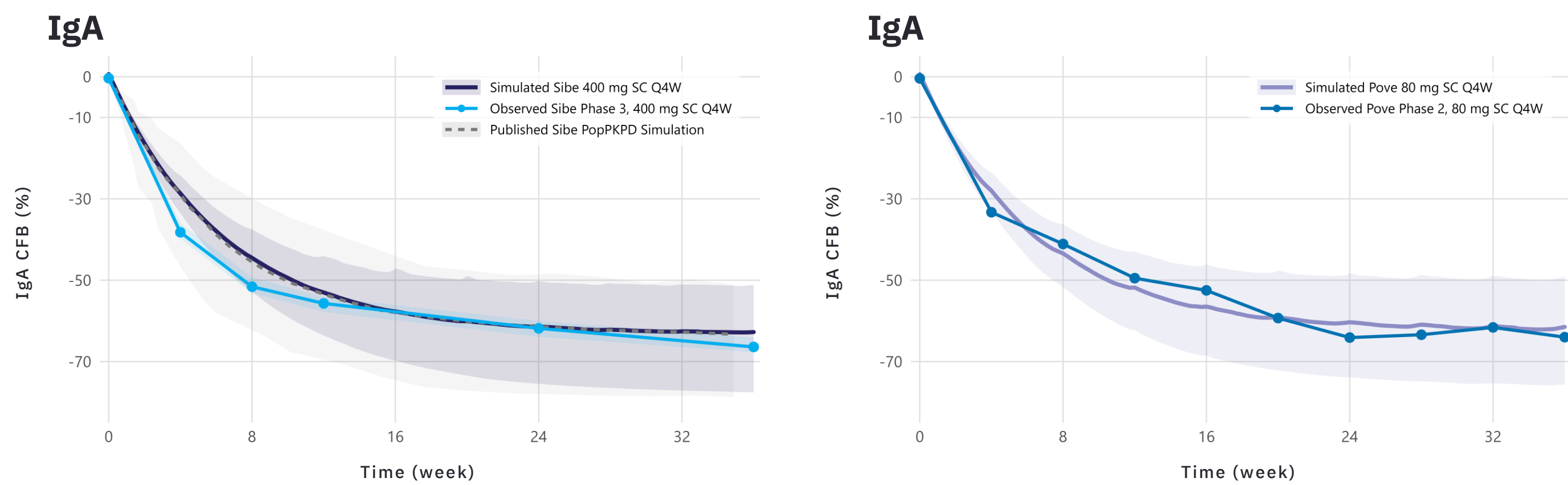


Figure 2. Integrated model qualification versus external observed IgA data. Solid lines and shaded areas denote the median and 95% prediction intervals (N=500 simulated individuals per scenario). Simulations generated internally using integrated PK-IgA models outlined above. Digitized observed mean data represented by blue dots connected by solid lines and digitized published sibiaprenlimab-IgA model outputs represented by dashed gray line and shaded area denoting the median and 95% prediction intervals (Pove: Tumlin, 2024 (WCN Poster); Sibe: Voyxact, 2025).

Model Predicted IgA and IgG Responses

JADE101 predicted to potentially lower IgA while relatively sparing IgG, consistent with the apparent maximum biological effects of the selective anti-APRIL mechanism of action on these clinically and translationally relevant biomarkers.

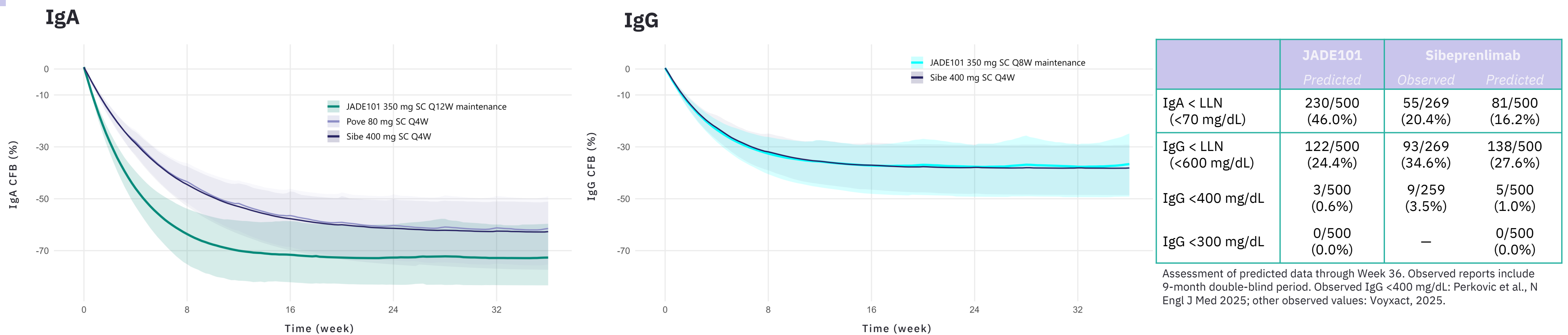


Figure 3 and Table 2. Solid lines and shaded area denote the median and 95% prediction intervals (N=500 simulated individuals per scenario). Simulations generated internally using integrated models outlined above. IgA and IgG models leverage the same generalized PKPD structure with molecule specific inputs. More intensive Q8W regimen shown for IgG safety comparison; less intensive Q12W shown for IgA clinical activity. Table presents the predicted and observed (where available) number and % of individual participants reaching specified IgA/IgG threshold levels at steady-state.

	JADE101 Predicted	Sibiaprenlimab Observed	Sibiaprenlimab Predicted
IgA < LLN (<70 mg/dL)	230/500 (46.0%)	55/269 (20.4%)	81/500 (16.2%)
IgG < LLN (<600 mg/dL)	122/500 (24.4%)	93/269 (34.6%)	138/500 (27.6%)
IgG <400 mg/dL	3/500 (0.6%)	9/259 (3.5%)	5/500 (1.0%)
IgG <300 mg/dL	0/500 (0.0%)	—	0/500 (0.0%)

Assessment of predicted data through Week 36. Observed reports include 9-month double-blind period. Observed IgG <400 mg/dL: Perkovic et al., N Engl J Med 2025; other observed values: Voyxact, 2025.

Integrated Assessment of PK-PD-UPCR Relationships

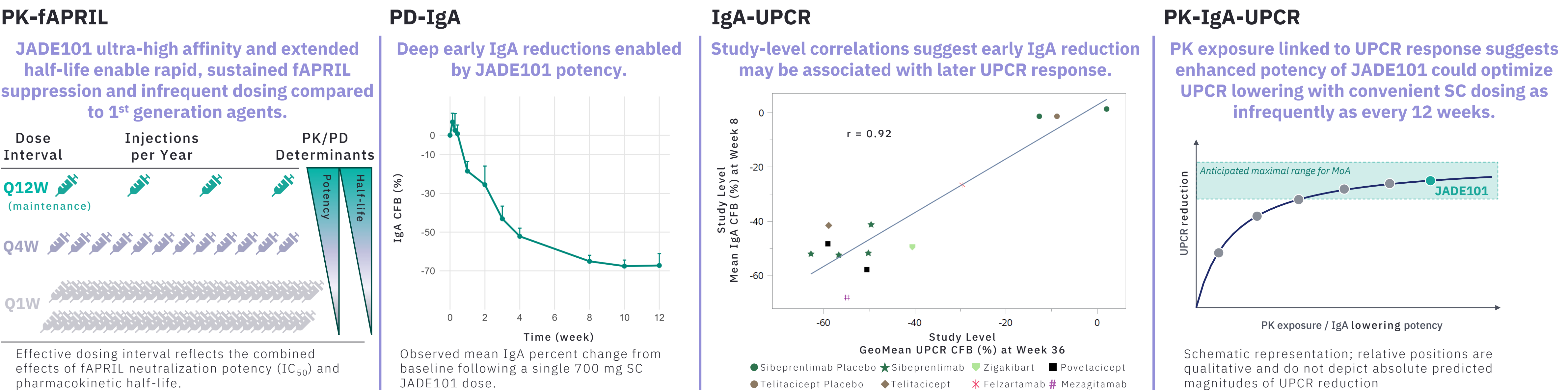


Figure 4. Integrative model-informed drug development framework informing JADE101 development as an APRIL targeted therapy in IgAN.

Data Sources

J A D E 1 0 1

Gufford B, DeVries T, Tong V, Lewis S, Kocinsky H, Li L, et al. SA-PO0272 A Translational Framework to Predict Clinical Responses to APRIL Blockade for Development of JADE101, an Anti-APRIL Monoclonal Antibody in IgAN. Journal of the American Society of Nephrology. 2025. 36(10S)

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Internal Data

P O V E T A C I C E P T

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S I B E P R E N L I M A B

VOYXACT Review; Center for Drug Evaluation and Research. Integrated Review: BLA 761434 VOYXACT (sibiaprenlimab-szsl). U.S. Food and Drug Administration; November 21, 2025. Application No. 761434Orig1s000.

Perkovic V, Trimarchi H, Tesar V, Lafayette R, Wong MG, Barratt J et al. Sibiaprenlimab in IgA Nephropathy-Interim Analysis of a Phase 3 Trial. New England Journal of Medicine. 2026 Feb 12;394(7):635-646.

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N O T E

Data digitized from available published tables and figures to approximate actual results. Jade does not possess the underlying raw third-party data. Model predicted data may not be realized in actual clinical studies and may not accurately represent performance of third-party products. These data are derived from different trials at different points in time, with differences in trial design, populations, and other factors. Caution should be exercised in drawing any conclusions from a comparison of the data across studies as cross-study comparisons are inherently limited and such data may not be directly comparable. No head-to-head clinical trials of JADE101 and other candidates or approved agents have been conducted.

Acknowledgements

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