WCN24-AB-2522
FRI-162

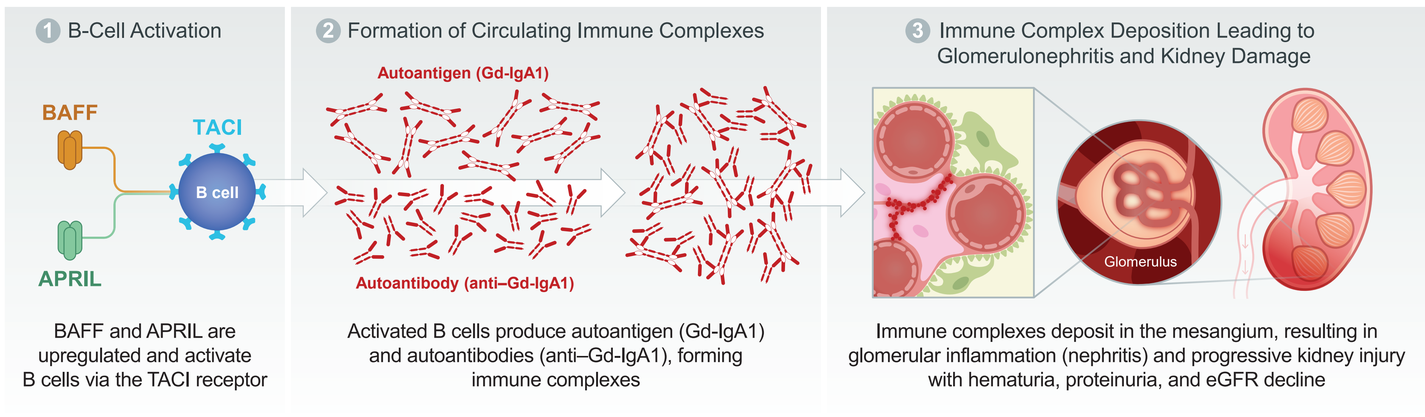
ORIGIN Extend: A Long-Term Extension Study of Atacicept in IgAN

Jonathan Barratt[1], Amit Sharma[2], Zeeshan Khawaja[2], Xuelian Wei[2], Richard Lafayette[3]

[1]University of Leicester, Leicester, UK; [2]Vera Therapeutics, Inc., Brisbane, United States; [3]Stanford University, Stanford, United States; on behalf of the ORIGIN Extend Study Team

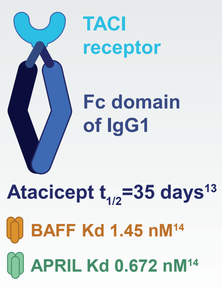
IgA Nephropathy: B-Cell–Mediated Kidney Disease With High Unmet Need for Safe and Effective Disease-Modifying Therapies[1-3]

- IgAN is associated with a relentless loss of kidney function and high lifetime risk of kidney failure[4]
- IgAN is predominantly diagnosed in young adults; most patients already show signs of CKD at diagnosis and approximately 50% require dialysis or transplant within 10–20 years of diagnosis[5-7]
- IgAN is associated with key biomarkers of disease: increased serum Gd-IgA1 levels, hematuria, proteinuria, and eGFR decline[8]
- Current treatment options have not been shown to reduce the rate of eGFR decline to a level that minimizes the lifetime risk of kidney failure[9,10]



APRIL = a proliferation-inducing ligand; BAFF = B-cell activating factor; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; Gd-IgA1 = galactose-deficient immunoglobulin A1; IgAN = IgA nephropathy; TACI = transmembrane activator and calcium-modulator and cyclophilin ligand interactor.

Atacicept: Dual BAFF/APRIL Inhibitor With Disease-Modifying Potential in Clinical Development



Atacicept $t_{1/2}$=35 days[13]

BAFF Kd 1.45 nM[14]

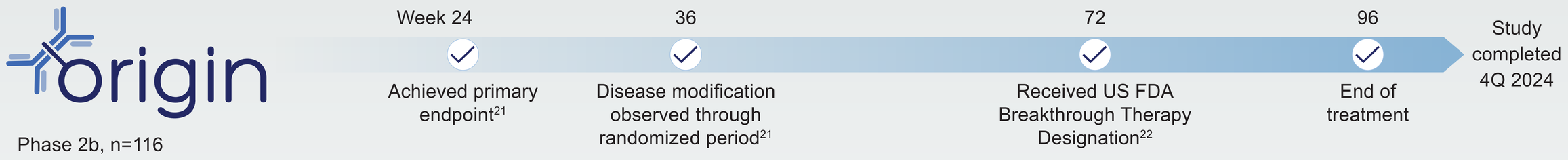
APRIL Kd 0.672 nM[14]

- Rational drug design: fully humanized TACI-Fc fusion protein resulting in a soluble receptor for cytokines BAFF and APRIL[1,11,12]
- Precision B-cell modulator that reduces expression of both the pathogenic autoantigen (Gd-IgA1) and autoantibody (anti–Gd-IgA1)[1,11,12]
- Half-life of 35 days with nanomolar potency for binding BAFF and APRIL[13,14]
- At-home self-administration of 1 mL SC weekly injection

Fc = fragment crystallizable region; IgG1 = immunoglobulin G1; Kd = dissociation constant; SC = subcutaneous; $t_{1/2}$ = half-life.

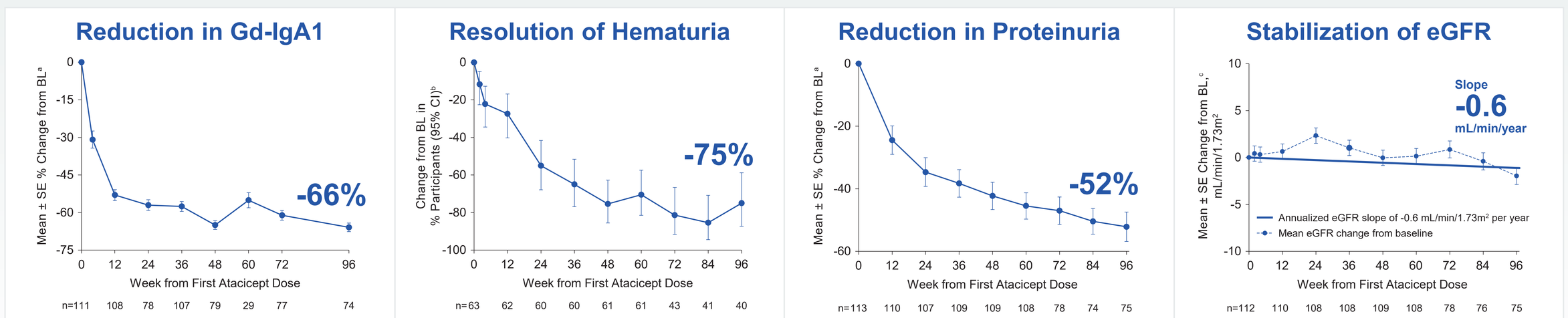
- BAFF and APRIL are the two main drivers of B-cell overproduction of Gd-IgA1 and anti–Gd-IgA1 autoantibodies and have redundant and overlapping functions[1,15,16]
- In animal models, dual inhibition has been shown to better mitigate disease progression than single inhibition[17]
- Dual inhibition may prevent compensatory increases in signaling[1,18,19]
- Inhibiting APRIL alone could lead to upregulation of BAFF, potentially affecting treatment efficacy[20]

Atacicept Clinical Development Program in IgAN



Long-Term Results Consistent With Disease-Modifying IgAN Profile[23]

Data From First Dose of Atacicept Through 96 Weeks



Atacicept group includes all participants who received any atacicept dose at any timepoint, with baseline (BL) defined as the last available measurement prior to the first dose of atacicept. Data from weeks 0 to 60 include participants who switched from placebo to atacicept. [a]Percentage changes from BL computed using FDA-endorsed mixed-effects modeling; [b]Percentages represent change from BL in number of participants with hematuria (urine dipstick blood ≥ 1+) at each visit divided by number of participants with BL hematuria shown on the lower axis; resolution defined as urine dipstick blood of trace or negative; [c]Changes from BL in eGFR were analyzed using mixed-effects model for repeated measures (MMRM) analysis and least-squares estimation and standard error (SE) were estimated from the model directly; eGFR slope was analyzed using mixed-effects model with random intercept and random slope, and mean slope and SE were estimated from the model directly. CI = confidence interval. ClinicalTrials.gov NCT04716231.

origin 3

Phase 3 pivotal trial, n≈376

Completed enrollment for primary endpoint[24]

Study enrolling

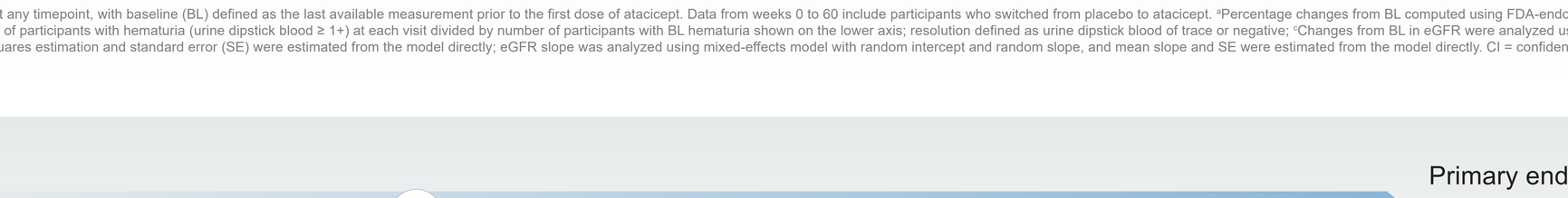
Primary endpoint available 2Q 2025

Consistent with Phase 2b: study design, patient population, atacicept dose, and SC formulation

ClinicalTrials.gov NCT04716231.

origin extend

Commitment to providing long-term access to atacicept for all ORIGIN participants



- Phase 2 extension study in participants who complete ORIGIN 2b or ORIGIN 3
- Objectives:
  1. Provide patients with extended access to atacicept prior to commercial availability in their country or region
  2. Capture longer-term data for research purposes
  3. Generate data from reinitiation of atacicept treatment following off-treatment period

ClinicalTrials.gov NCT06674577.

Inclusion Criteria

- Completed the protocol-defined treatment period on treatment in a parent study of atacicept in patients with IgAN

Key Endpoints

- Evaluate the long-term efficacy and safety of atacicept:
  - Changes in serum Gd-IgA1 levels
  - Changes in hematuria
  - Changes in proteinuria
  - Changes in eGFR
  - Safety and adverse events

Learn more about the ORIGIN clinical program at theORIGINiganstudy.com or contact us at clinicaltrials@veratx.com

References: **1.** Cheung CK, et al. Front Nephrol. 2024;3:1346769; **2.** Huang X, Xu G. Front Pharmacol 2021;12:715253; **3.** Popova A, et al. Nephrol Dial Transplant 2024;gfae173; **4.** Wyatt RJ, Julian BA. N Engl J Med 2013;368:2402-14; **5.** Jarrick S, et al. J Am Soc Nephrol 2019;30:866-76; **6.** Kwon CS, et al. J Health Econ Outcomes Res 2021;8:36-45; **7.** Pitcher D, et al. Clin J Am Soc Nephrol 2023;18:727-38; **8.** Duan ZY, et al. Biomark Res 2024;12:72; **9.** Lafayette R, et al. Lancet 2023;402(10405):859-870; **10.** Rovin BH, et al. Lancet 2023;402(10417):2077-2090; **11.** Gordon C, et al. Rheumatol Adv Pract 2019;3:rkz021; **12.** Carbonatto M, et al. Toxicol Sci 2008;105:200-10; **13.** Willen D, et al. Eur J Drug Metab Pharmacokinet 2020;45:27-40; **14.** Vera data on file; **15.** Xu S, et al. Cancers 2020;12:1045; **16.** Benson M, et al. J Immunol 2008;180:3655-9; **17.** Haselmayer P, et al. Eur J Immunol 2017;47:1075-85; **18.** Yeh T, et al. J Allergy Clin Immunol 2020;146:1109-20.e4; **19.** Tsiantoulas et al. Nature 2021;597:92-6; **20.** Vallerskog T, et al. Arthritis Res Ther 2006;8:R167; **21.** Lafayette R, et al. Kidney Int. 2024;S0085-2538(24)00236-9; **22.** Vera Therapeutics news release: https://ir.veratx.com/news-releases/news-release-details/vera-therapeutics-receives-us-fda-breakthrough-therapy; **23.** Barratt J, et al. J Am Soc Nephrol 2024 Oct 26:10.1681/ASN.0000000541; **24.** Vera Therapeutics news release https://ir.veratx.com/news-releases/news-release-details/vera-therapeutics-completes-enrollment-primary-endpoint-pivotal.

Acknowledgments: We thank the ORIGIN Phase 2b and Phase 3 study volunteers and their families, and the ORIGIN investigators, study staff, and collaborators.

SCAN TO DOWNLOAD

Contact: medinfo@veratx.com

2000 Sierra Point Parkway, Suite 1200, Brisbane, CA 94005 I (650) 770-0077

vera therapeutics™

© 2025 Vera Therapeutics, Inc.