Felzartamab (anti-CD38 antibody) for the Treatment of Lupus Nephritis – An Open Label Phase 1b Study

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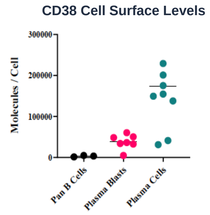
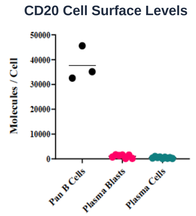
Lupus Nephritis (LN) and the potential for anti-CD38 therapy

- LN is the most common major organ-threatening manifestation of systemic lupus erythematosus (SLE) that affects ~35-60% of SLE patients
- Only 30-40% of LN patients achieve complete renal response with current standard of care therapy
- A hallmark of LN is high-titer autoantibodies (eg, anti-dsDNA, anti-Smith) which are predominantly produced by CD38+ plasma cells
- CD38 expression is also induced on plasmacytoid Dendritic Cells (pDCs), the primary source of Type I IFN that has been also implicated in the pathogenesis of SLE
- CD38 is thus a compelling target for depletion of pathogenic cells in LN, supported by emerging clinical data that anti-CD38 therapy in LN is well tolerated with evidence of disease improvement or resolution.

CD38 is Upregulated in Plasma Cells and pDCs in SLE





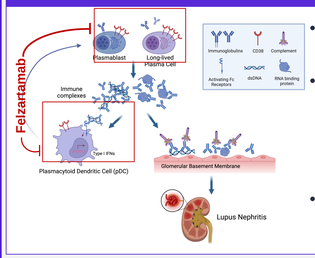
- CD38 cell surface expression is elevated in plasma cells and plasmablasts compared to earlier B cells whereas CD20 expression is lost on plasmablasts and plasma cells (left)
- Additional published evidence that CD38 gene expression in plasmablasts and pDCs is elevated in SLE compared to healthy controls

Case Reports for Safety & Efficacy of anti-CD38 in SLE/LN

Publication	Patients	Clinical Outcomes	Safety	Other Key Biomarkers
Roccatello et al, Nature Medicine 2023	N = 6, refractory Lupus Nephritis	• 5/6 renal remission (3 CRR, 2 PRR) by 1yr • Improvement in SLEDAI 2K	• No SAEs	• Decrease in IFN-Gamma, sCD163, anti-dsDNA, C4
Ostendorf et al, NEJM 2020	N = 1 hematologic SLE; N = 1 severe active LN	• Improvement in SLEDAI-2K (clinical) scores, urinary proteins and serum creatinine	• 1 AE upper respiratory tract infection	• Decrease in serum anti-dsDNA titers

Felzartamab is a fully human anti-CD38 antibody in development for immune-mediated kidney diseases

Felzartamab Proposed Mechanism of Action in LN



- Felzartamab is a recombinant human IgG mAb that binds the CD38 cell surface antigen with high affinity
- Felzartamab depletes CD38 high antibody-producing cells such as plasma cells/plasmablasts primarily via antibody-dependent cell-mediated cytotoxicity (ADCC) and antibody-dependent cell-mediated phagocytosis (ADCP), with minimal impact of complement-dependent cytotoxicity (CDC)
- In SLE/LN, felzartamab may also deplete plasmacytoid dendric cells (pDCs) that contribute to disease via Type I Interferon production

- Beyond LN, felzartamab is in development for several immune mediated kidney diseases, including primary membranous nephropathy (PMN), IgA nephropathy, and Ab-mediated kidney transplant rejection
- Felzartamab is well tolerated across clinical studies in immune mediated diseases with encouraging evidence of CD38+ cell depletion and lowering autoantibodies, while maintaining the ability for patients to mount humoral response to vaccines
- In studies of high-risk PMN pts, felzartamab resulted in rapid, deep, and durable aPLA2R autoantibody responses with associated improvements in proteinuria and serum albumin.
- For further information on felzartamab, see:
  - Oral Presentation: "Safety and Efficacy of Felzartamab in Primary Membranous Nephropathy (PMN): Final Analysis of the M-PLACE Study". November 2, 2023; from 5:24 PM to 5:33 PM; Room 103
  - Poster Presentation: "Felzartamab reduces aPLA2R Ab by selectively depleting CD38+ plasma cells and plasmablasts, the main pathogenic cellular drivers of disease in Primary Membranous Nephropathy (PMN)". November 4, 2023; from 10:00 AM to 12:00 PM.

For more information about the trial, scan here:

Acknowledgments and Disclosures

This study is sponsored and funded by HI-Bio Inc.

About felzartamab

Felzartamab is an investigational drug that has not yet been approved by any regulatory authorities.

HI-Bio in-licensed felzartamab from MorphoSys in June 2022, and holds exclusive worldwide rights for felzartamab with the exception of Greater China. In 2017, MorphoSys entered into an exclusive regional licensing agreement with I-Mab Biopharma to develop and commercialize felzartamab in Greater China. I-Mab is evaluating felzartamab in relapsed/refractory multiple myeloma.

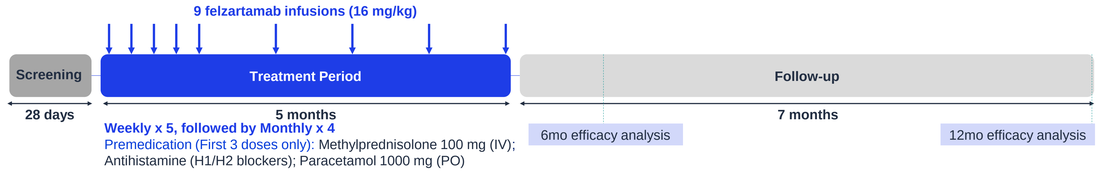
Conflicts of interest

BHR: consulting fees from HI-Bio; **LDP, UDP, KT:** Employees of HI-Bio Inc., with stock or stock options; **EM:** consulting fees from HI-Bio; **MDE:** consulting fees from HI-Bio

LN P1b (NCT# 06064929)

Phase 1b, open-label, trial to assess the safety, efficacy and PK/PD of felzartamab in patients with refractory Lupus Nephritis

Study Protocol



- ~20 pts in US, Canada, Australia, Argentina, Chile, and Mexico with SLE and Class III or IV +/- V LN
- Allowable medications for LN: a) Mycophenolate up to 3 g/day; b) Azathioprine up to 2 mg/kg/day; c) Corticosteroids up to 20 mg/day
- Protocol-prohibited medications for LN: a) Calcineurin inhibitors (e.g., cyclosporine, tacrolimus, or voclosporin); b) Alkylating agents, including cyclophosphamide; c) Biologic agents

Outcome Measures

Primary Endpoint

- Safety and tolerability of felzartamab as assessed by incidence and frequency of treatment-emergent adverse events (TEAEs), including SAEs

Secondary Endpoints

- Change from baseline in lupus serologic markers: C3 & anti-dsDNA
- Change from baseline in UPCR
- Renal response (CRR, PRR) at Week 24 and 52
- Change from baseline in serum creatinine, urine protein, eGFR

Key Eligibility Criteria

Inclusion

- Adult male or female, 18 to 75y/o
- SLE according to the EULAR/ ACR criteria
- Class III or IV +/- V LN by renal biopsy within 1 year prior to screening
- UPCR > 1.0 g/g on 24h urine collection
- Positive anti-dsDNA and/or low C3 during screening
- Inadequate response/intolerance to at least a 3-month course of one SOC treatment for LN

References: Burns M, Ostendorf L, Biesen R, et al. Dysregulated CD38 Expression on Peripheral Blood Immune Cell Subsets in SLE. Int J Mol Sci. 2021;22(5):2424. Published 2021 Feb 28.● Ostendorf L, Burns M, Durek P, et al. Targeting CD38 with Daratumumab in Refractory Systemic Lupus Erythematosus. N Engl J Med. 2020;383(12):1149-1155 ● Roccatello, D., Fenoglio, R., Caniggia, I. et al. Daratumumab monotherapy for refractory lupus nephritis. Nat Med 29, 2041–2047 (2023) ● Rovin BH, Boxhammer R, Thakur A, Ronco PM. Immunologic Responses After COVID-19 Vaccination in Patients With Membranous Nephropathy Receiving Anti-CD38 Felzartamab Therapy: Results From the Phase 1b/2a M-PLACE Study. Kidney Int Rep. 2022;7(9):2086-2090; Sterner RM, Hartono SP, Grande JP. The Pathogenesis of Lupus Nephritis. J Clin Cell Immunol. 2014 Apr;5(2):205.