Q32 BIO

Building The Future of Immune Therapeutics

Company Overview

January 2025

Forward Looking Statements

This presentation has been prepared by Q32 Bio Inc. ("we", "us," "our," "Q32" or the "Company") and is made for informational purposes only. The information set forth herein does not purport to be complete or contain all of the information you may desire. Statements contained herein are made as of the date of this presentation unless stated otherwise, and this presentation shall not under any circumstances create an implication that the information contained herein is correct as of any time after such date or that information will be updated or revised to reflect information that subsequently becomes available or changes occurring after the date hereof.

This presentation contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," "potential," and similar expressions regarding future periods. These forward-looking statements include, but are not limited to, our beliefs, observations, expectations and assumptions regarding the topline data from the SIGNAL-AA Phase 2a and the safety, tolerability, clinical activity including biomarker data, potential efficacy and potential benefits of bempikibart, plans and expectations for Part B of the SIGNAL-AA Phase 2a clinical trial statements regarding expected cash and the sufficiency of the Company's cash to fund operations into mid- 2026, the expectations surrounding the potential, safety, efficacy, and regulatory and clinical progress of Q32's product candidates, including bempikibart and ADX-097, and anticipated milestones, data readouts and timing, among others. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the Company's need for additional funding, which may not be available; failure to identify additional product candidates and develop or commercialize marketable products; the early stage of the Company's development efforts; potential unforeseen events during clinical trials could cause delays or other adverse consequences; risks relating to the regulatory approval process; interim, topline and preliminary data may change as more patient data become available, and are subject to audit and verification procedures that could result in material changes in the final data; Q32's product candidates may cause serious adverse side effects; inability to maintain our collaborations, or the failure of these collaborations; our reliance on third parties, including for the manufacture of materials for our research programs, preclinical and clinical studies; failure to obtain U.S. or international marketing approval; ongoing regulatory obligations; effects of significant competition; unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives; product liability lawsuits; securities class action litigation; the impact of the COVID-19 pandemic and general economic conditions on our business and operations, including our preclinical studies and clinical trials; the possibility of system failures or security breaches; risks relating to intellectual property and our ability to protect our patents and other proprietary rights; significant costs incurred as a result of operating as a public company; as well as those risk and uncertainties set forth more fully under the caption "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2024 as well as other risks detailed in our subsequent filings with the United States Securities and Exchange Commission. Any forward-looking statement made by us is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

Certain information contained in this presentation relates to or is based on studies, publications, analyses, surveys and other data obtained from third-party sources and the Company's own internal estimates and research. While the Company believes these third-party sources to be reliable as of the date of this presentation, it has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, while we believe our own internal research is reliable, such research may not have been verified by any independent source.

Q32 Mission: Building The Future of Immune Therapeutics

Bempikibart (ADX-914)

IL-7Rα Antagonist Antibody
Dual IL-7/TSLP inhibition

- Proof of concept (POC) demonstrated in alopecia areata (AA) in Phase 2a Part A; high unmet need where treatments include JAK inhibitors which have class-wide safety warnings, a significant limitation for the AA patient demographic
- Meaningful hair regrowth with evidence of durability after 24-week treatment period with subcutaneous (SC) dosing
- Potential to transform AA treatment paradigm with durable effect and favorable tolerability and safety profile
- Phase 2a Part B to commence in 1H'25 with data in 1H'26; anticipated final step prior to pivotal trials
- Broad expansion opportunity in Th1 and Th2 mediated diseases supported by biomarker and T-cell changes

Novel Tissue-targeted Complement Platform

Lead Clinical Asset: ADX-097
Inactivates alternative pathway convertases

- Platform: Differentiated, targeted approach to address complement dysregulation directly in the tissue
- ADX-097: Clinical data to date show attainment of dose-dependent target PK/PD, favorable tolerability and good immunogenicity profile with SC dosing
- ADX-097: Phase 2 renal basket trial in IgAN, C3G and Lupus Nephritis ongoing

Near Term Value Creation Potential

Multiple near-term milestones

- 1H'25 – Bempikibart: Initiate enrollment in SIGNAL-AA Phase 2a Part B
- 1H'26 – Bempikibart: SIGNAL-AA Phase 2a Part B Topline Results
- 1H'25 – ADX-097: Renal basket Phase 2 Initial Data
- 2H'25 – ADX-097: Renal basket Phase 2 Topline Results

Exceptional Team

- Management team with extensive public biotech experience
- Deep inflammatory/autoimmune expertise including complement therapeutics

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Q32 Pipeline: Poised to Deliver Multiple Near-term Clinical Readouts

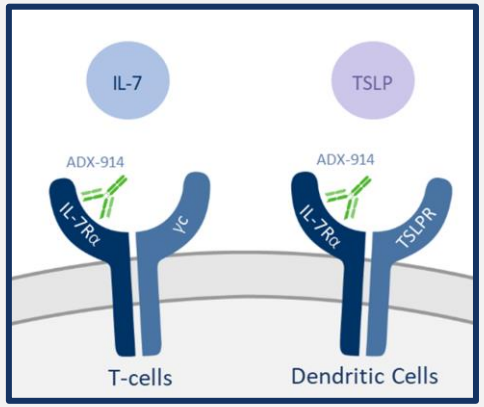
Program	Indication	Discovery/ Preclinical	Phase 1	Phase 2	Anticipated Milestones
IL-7/TSLP PROGRAM					
Bempikibart[1] (ADX-914)	Alopecia Areata				*Initiate Part B enrollment 1H'25; Topline data expected 1H'26*
COMPLEMENT INHIBITOR PLATFORM					
ADX-097	Renal Basket (IgAN, LN, C3G)				*Topline data expected 2H'25*

Note: IgAN = IgA Nephropathy; LN = Lupus Nephritis; C3G = C3 Glomerulopathy.

Bempikibart (ADX-914)
(IL-7 / TSLP Receptor Inhibitor)

Bempikibart: Bifunctional Antibody for T-cell Mediated I&I Diseases With Demonstrated Activity in AA

Bempikibart IL-7Rα antagonist antibody:
Blocks IL-7 and TSLP signaling



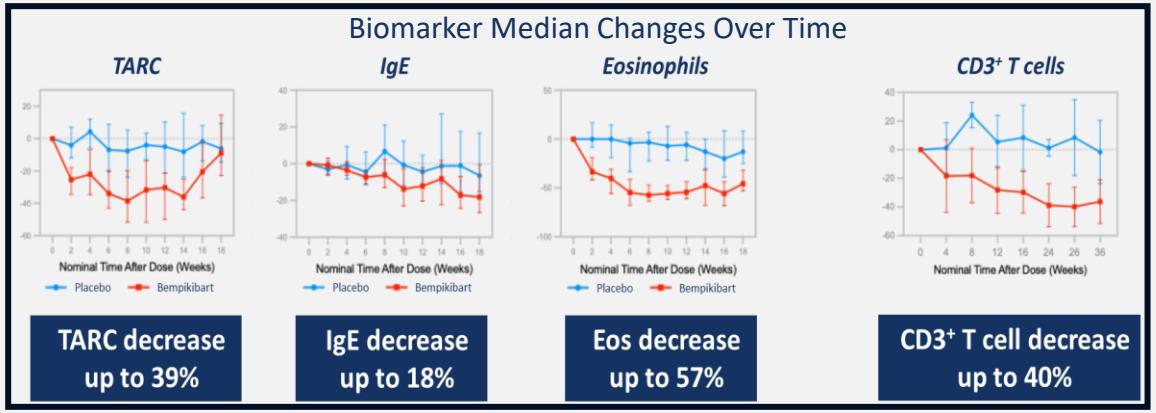
IL-7 receptor

- IL-7 regulates pathogenic T_{eff} / T_{mem} cells that suppress T_{reg} cells in preclinical models
- Blockade of IL-7Rα provides a novel mechanism for rebalancing $T_{eff/mem}$ and T_{reg} function

TSLP receptor

- TSLP is central regulator of dendritic cell differentiation, Th2 cytokines
- Blockade of TSLP function has potential to inhibit Th2 mediated inflammation and eosinophilic disease

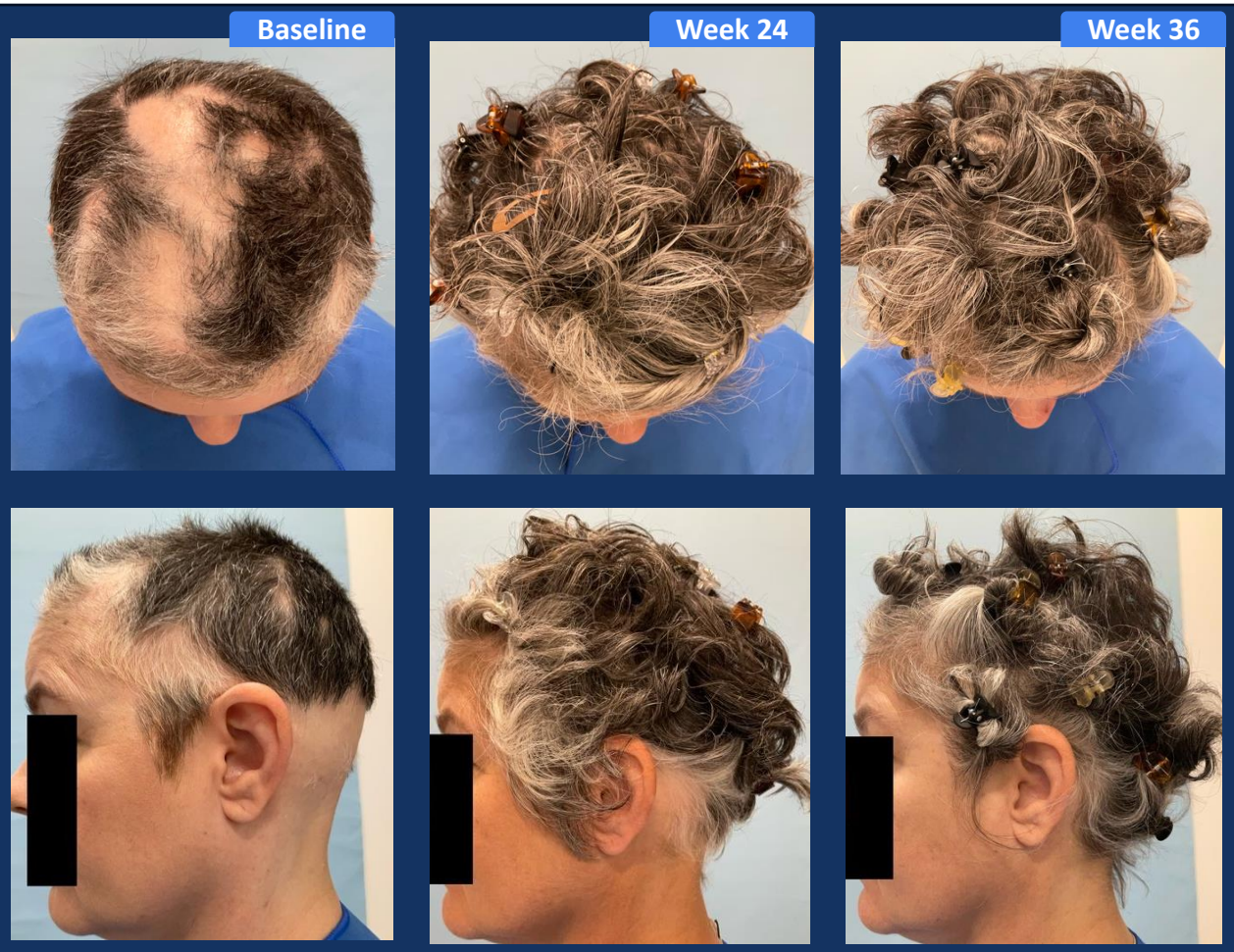
Biomarker changes and clinical activity in Phase 2a:
Supports IL-7Rα antagonist approach

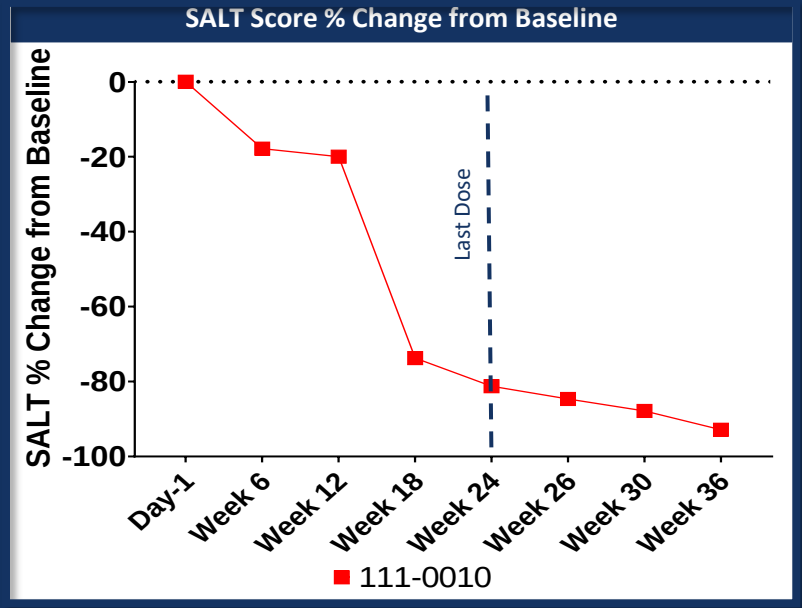


Clinical Data Across Phase 1 and Phase 2a

- Favorable PK/RO/PD and minimal ADA
- Mechanism demonstrated by changes in Th2 biomarkers and T cells supporting additional indication expansion opportunity beyond AA
- Well-tolerated safety profile across 130 subjects to date
- POC demonstrated with durable hair growth in AA in SIGNAL-AA Part A 24-week treatment and additional 12-week follow-up

SIGNAL-AA Case Study - Severe AA with 4.5 Year Episode Showing SALT-10 at Week 36: Supports Potential for Durable Hair Regrowth with Bempikibart Treatment





- 52-year-old female
- Duration of episode: 4.5 years
- Baseline SALT: 56
- SALT (Week 24): 10.5
- SALT (Week 36): 4

Durable response at Week 36; PI reports continued hair growth following completion of study

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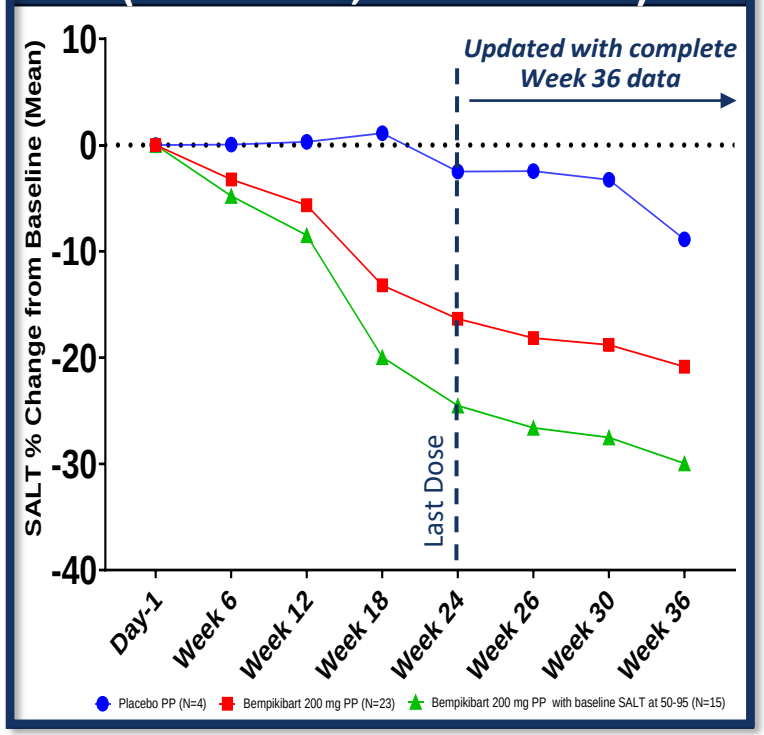
SIGNAL-AA: Part A SALT Data Through Week 36 Follow-up Showed Continued Benefit Over Time Supporting Potential for Remittive Effect Following Dosing Cessation

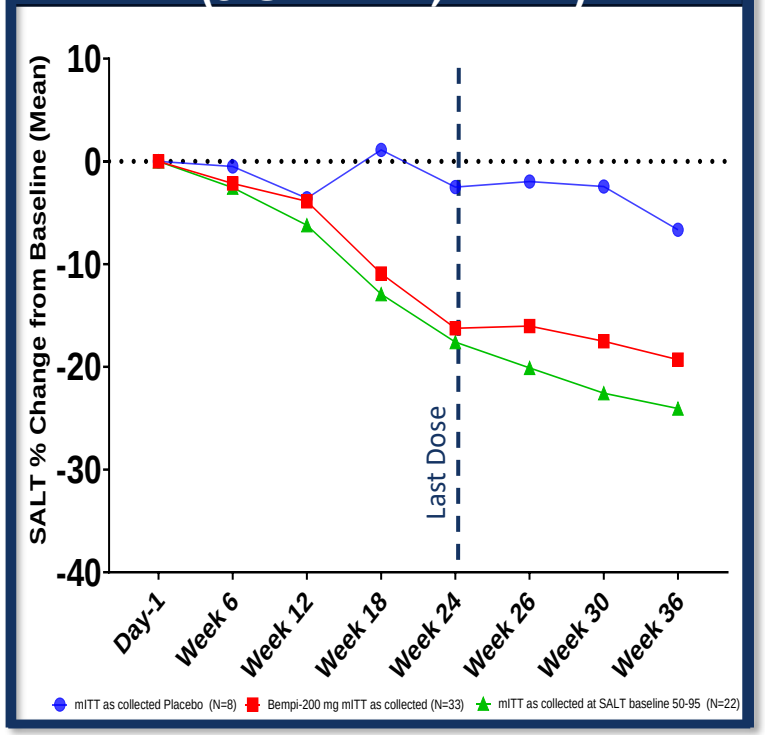
SALT Percentage Change Over Time (SIGNAL AA, Per Protocol[1])

	Week 24 (EOT)	Week 36[2,3] (EOS)
SEVERE AND VERY SEVERE SALT 50-100 (n=23 at Week 24)		
Mean SALT % Δ	16%	21%
SALT 30%	17%	39%
SALT-20	9%	6%
SEVERE ONLY SALT 50-95 (n=15 at Week 24)		
Mean SALT % Δ	25%	30%
SALT 30%	27%	58%
SALT-20	13%	8%

SALT Percentage Change Over Time (SIGNAL AA, Per Protocol[1])



SALT Percentage Change Over Time (SIGNAL AA, MITT[1])



Mean SALT reduction continues after dosing cessation, suggestive of potential for remittive effect. Response relevance supported by multiple inbound patient requests for continued dosing.

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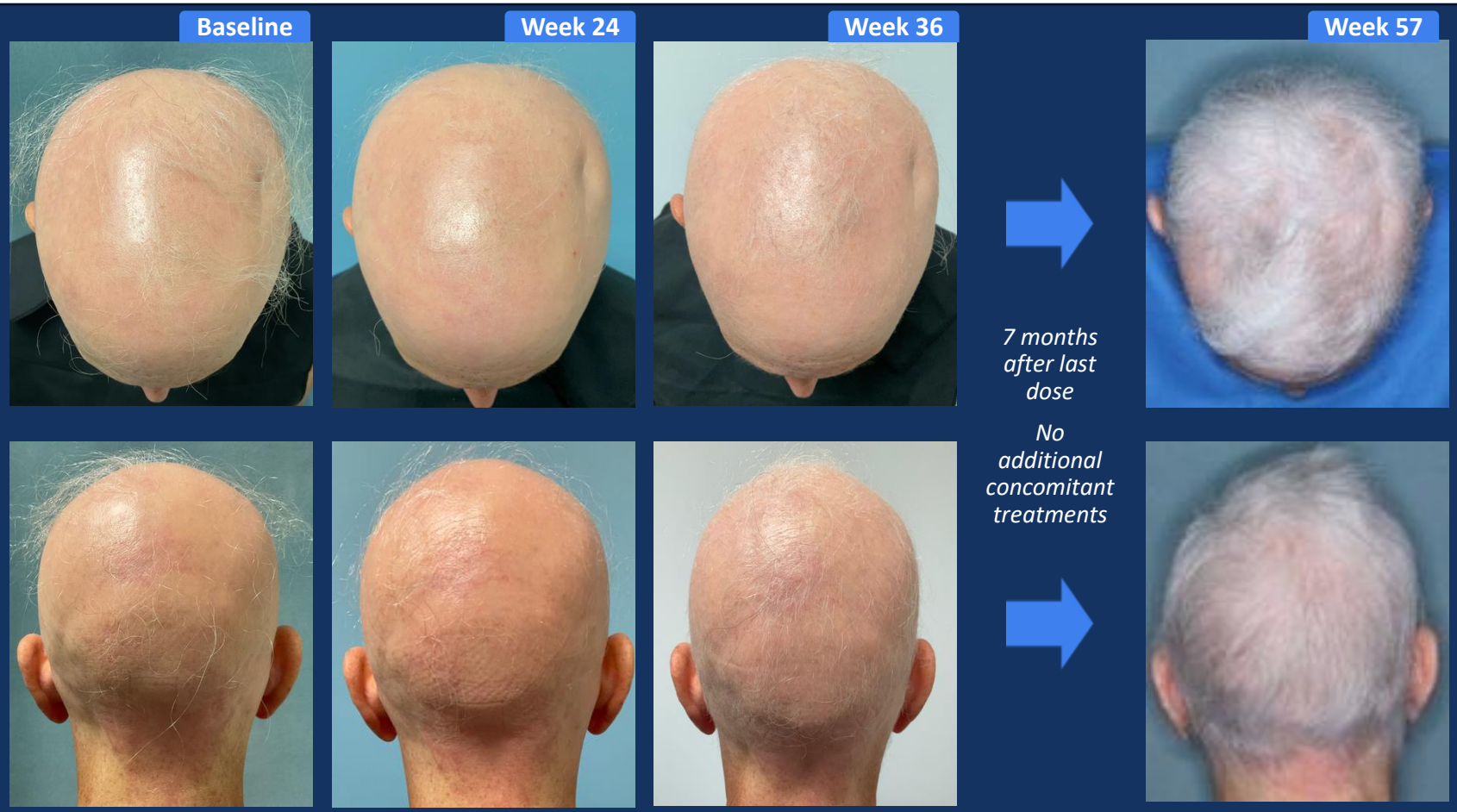
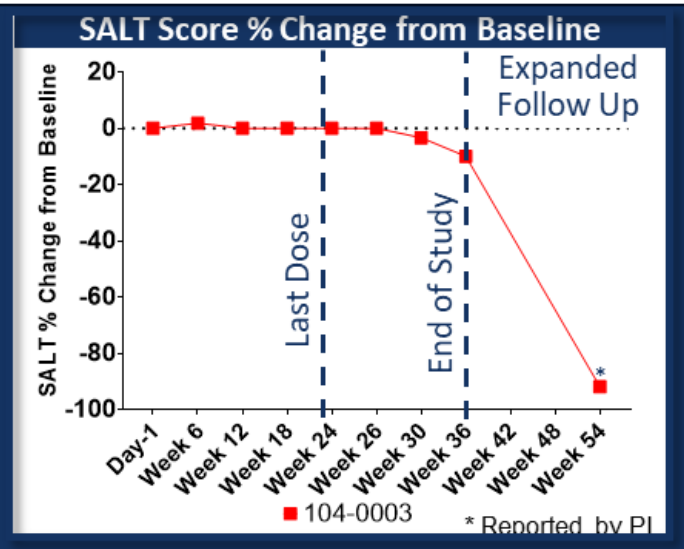
[1]Analysis excludes 3 placebo subjects from a single site who were major violations of inclusion criteria (AA diagnosis incorrect). Step Down Between mITT to Per Protocol: 10 early terminations, 2 missed week 24 visit, 1 missed multiple doses, 1 major hairstyle change. [2] 5 LTFU by wk36, [3] 3 LTFU by wk 36

SIGNAL-AA Case Study- Very Severe AA with SALT-10 Response After Dosing Cessation: Supports Potential for Remittive Effect with Bempikibart Treatment





- 61-year-old female
- Duration of Episode: 3.1 years
- Baseline SALT: 98.2
- SALT (Week 24): 98.2
- SALT (Week 36): 88.4
- SALT (Week 54): 8

Achieved near complete hair regrowth ~7 months after last dose; Patient has requested additional dosing

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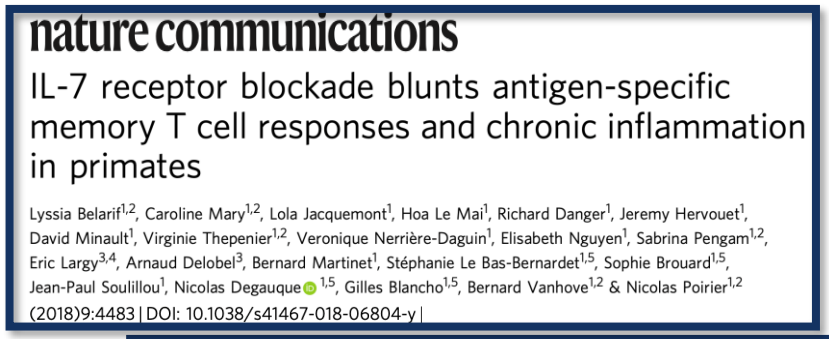
SIGNAL-AA First-in-Patient Observations of Durable Response Supported by Broad Literature Describing IL-7 Mechanistic Modulation of $T_{eff/mem}$ cells

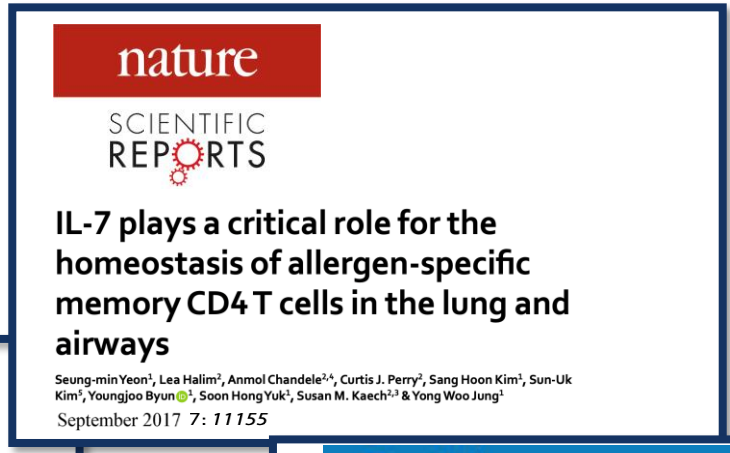


nature communications

IL-7 receptor blockade blunts antigen-specific memory T cell responses and chronic inflammation in primates

Lyssia Belarif[1,2], Caroline Mary[1,2], Lola Jacquemont[1], Hoa Le Mai[1], Richard Danger[1], Jeremy Hervouet[1], David Minault[1], Virginie Thepenier[1,2], Veronique Nerrière-Daguin[1], Elisabeth Nguyen[1], Sabrina Pengam[1,2], Eric Largy[3,4], Arnaud Delobel[3], Bernard Martinet[1], Stéphanie Le Bas-Bernardet[1,5], Sophie Brouard[1,5], Jean-Paul Soulillou[1], Nicolas Degauque[1,5], Gilles Blancho[1,5], Bernard Vanhove[1,2] & Nicolas Poirier[1,2]

(2018)9:4483 | DOI: 10.1038/s41467-018-06804-y |



nature SCIENTIFIC REPORTS

IL-7 plays a critical role for the homeostasis of allergen-specific memory CD4 T cells in the lung and airways

Seung-min Yeon[1], Lea Halim[2], Anmol Chandele[2,4], Curtis J. Perry[2], Sang Hoon Kim[1], Sun-Uk Kim[3], Youngjoo Byun[1], Soon Hong Yuk[1], Susan M. Kaech[2,3] & Yong Woo Jung[1]

September 2017 7: 11155

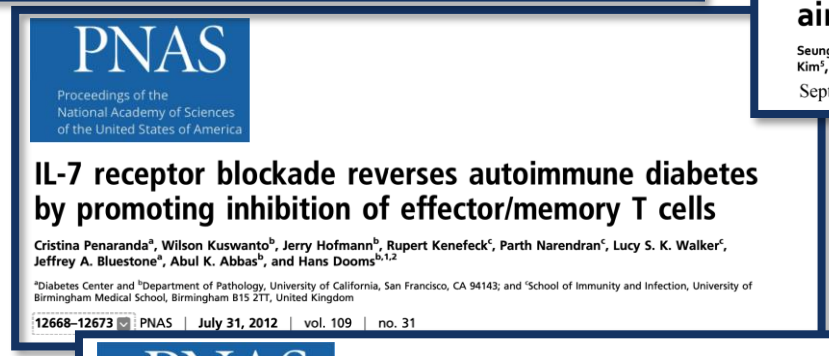
PNAS Proceedings of the National Academy of Sciences of the United States of America

Anti–IL-7 receptor-α reverses established type 1 diabetes in nonobese diabetic mice by modulating effector T-cell function

Li-Fen Lee[a,1], Kathryn Logronio[a], Guang Huan Tu[a], Wenwu Zhai[a], Irene Ni[a], Li Mei[a], Jeanette Dilley[a], Jessica Yu[a], Arvind Rajpal[a], Colleen Brown[a], Charles Appah[a], Sherman Michael Chin[a], Bora Han[b], Timothy Affolter[b], and John C. Lin[a,1]

[a]Rinat, Pfizer Inc., South San Francisco, CA 94080; and [b]Drug Safety R and D, Pfizer Inc., La Jolla, CA 92121

12674–12679 | PNAS | July 31, 2012 | vol. 109 | no. 31



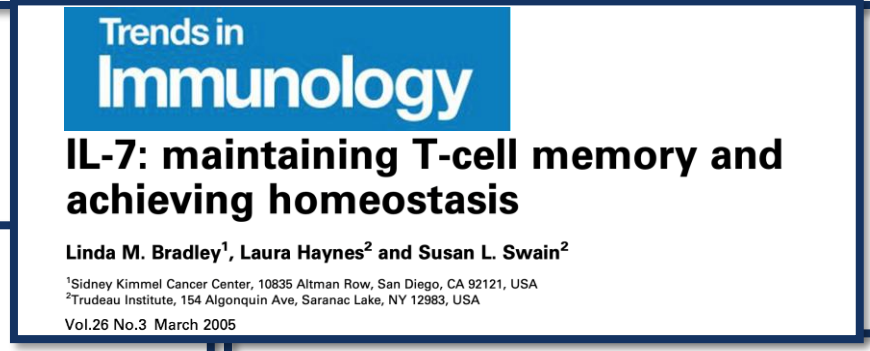
PNAS Proceedings of the National Academy of Sciences of the United States of America

IL-7 receptor blockade reverses autoimmune diabetes by promoting inhibition of effector/memory T cells

Cristina Penaranda[a], Wilson Kuswanto[b], Jerry Hofmann[b], Rupert Kenefeck[c], Parth Narendran[c], Lucy S. K. Walker[c], Jeffrey A. Bluestone[a], Abul K. Abbas[b], and Hans Dooms[b,1,2]

[a]Diabetes Center and [b]Department of Pathology, University of California, San Francisco, CA 94143; and [c]School of Immunity and Infection, University of Birmingham Medical School, Birmingham B15 2TT, United Kingdom

12668–12673 | PNAS | July 31, 2012 | vol. 109 | no. 31



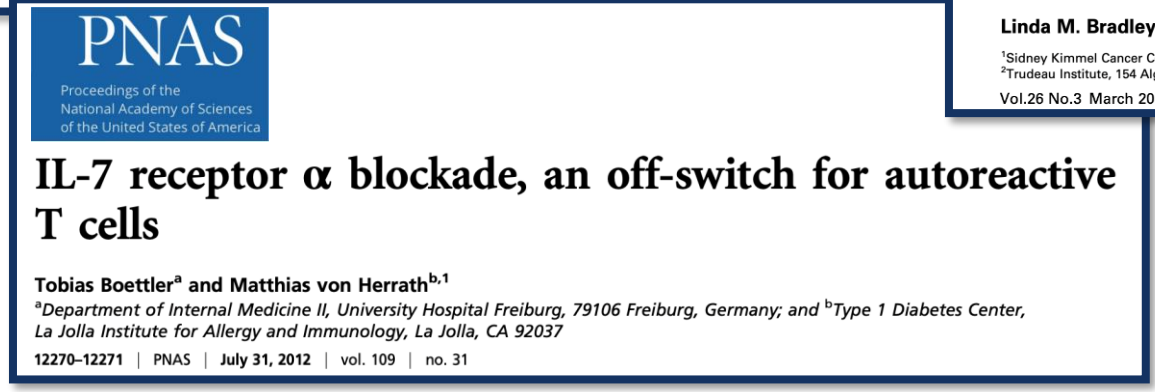
Trends in Immunology

IL-7: maintaining T-cell memory and achieving homeostasis

Linda M. Bradley[1], Laura Haynes[2] and Susan L. Swain[2]

[1]Sidney Kimmel Cancer Center, 10835 Altman Row, San Diego, CA 92121, USA
[2]Trudeau Institute, 154 Algonquin Ave, Saranac Lake, NY 12983, USA

Vol.26 No.3 March 2005



PNAS Proceedings of the National Academy of Sciences of the United States of America

IL-7 receptor α blockade, an off-switch for autoreactive T cells

Tobias Boettler[a] and Matthias von Herrath[b,1]

[a]*Department of Internal Medicine II, University Hospital Freiburg, 79106 Freiburg, Germany; and* [b]*Type 1 Diabetes Center, La Jolla Institute for Allergy and Immunology, La Jolla, CA 92037*

12270–12271 | PNAS | July 31, 2012 | vol. 109 | no. 31

The Journal of Immunology

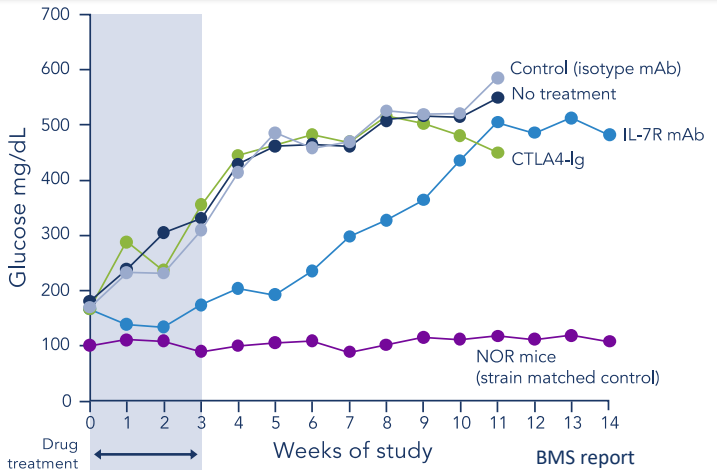
RESEARCH ARTICLE | DECEMBER 15 2012

IL-7 Abrogates Suppressive Activity of Human $CD4^+CD25^+FOXP3^+$ Regulatory T Cells and Allows Expansion of Alloreactive and Autoreactive T Cells FREE

Anne-Kristin Heninger; ... et. al

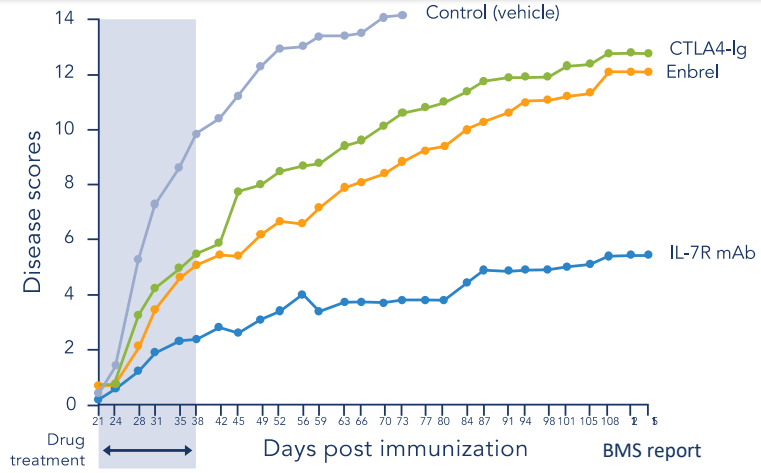
Preclinical Evidence of Long-Term Durable Effects Following IL-7Rα Antibody Treatment: Models Suggest a Mechanism for Rebalancing $T_{eff/mem}$ and T_{reg} function

Type 1 Diabetes Model



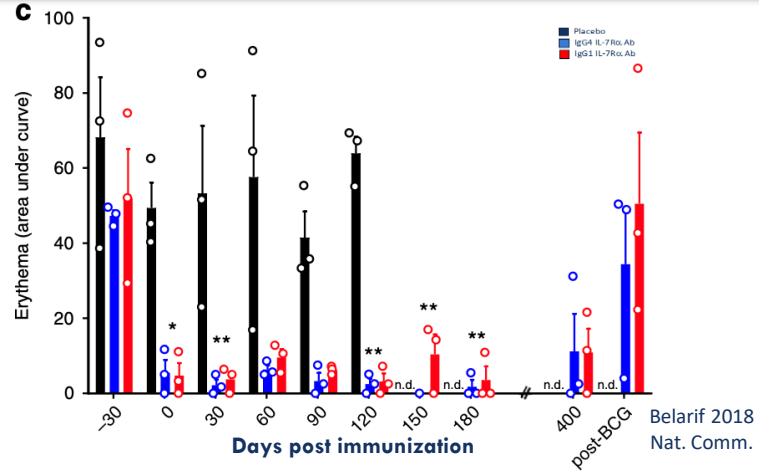
- Anti-IL-7Rα treatment markedly reduces/delays diabetes onset in NOD1 mice
- Effect persists 7+ weeks after secession of dosing

Collagen Induced Arthritis Model



- Anti-IL-7Rα treatment markedly reduces collagen induced arthritis in mice
- Effect persists 10+ weeks after secession of dosing

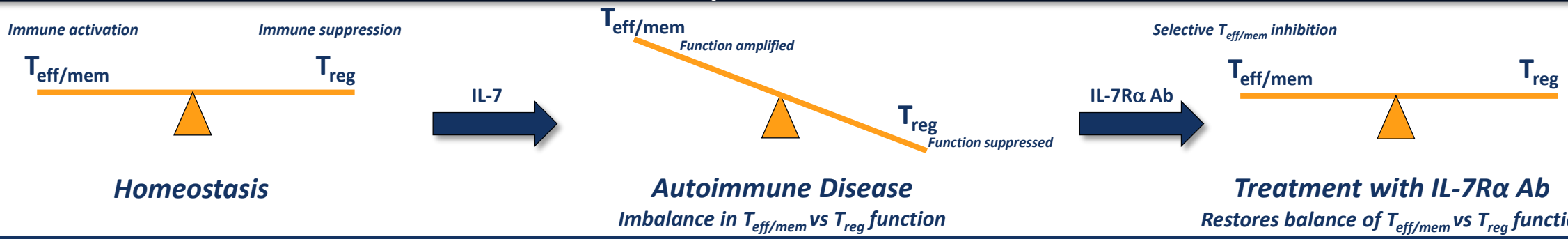
Tuberculin Challenge Model



Belarif 2018 Nat. Comm.

- One dose of anti-IL-7Rα markedly reduces tuberculin induced DTH response in baboons
- Effect persists for 1+ year, BCG vaccine restores response

Proposed Mechanism



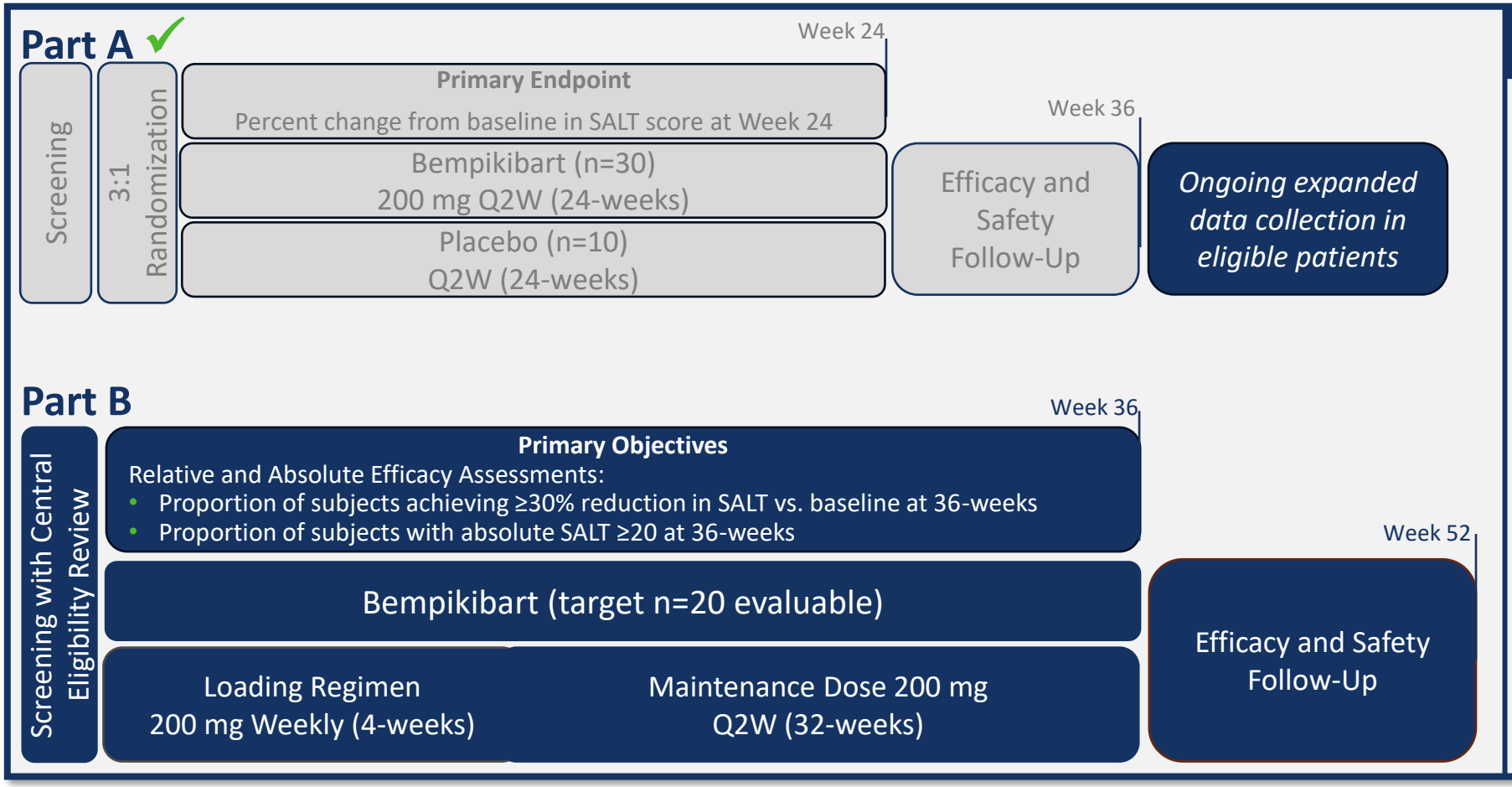
Maturing SIGNAL-AA Data Package Supports Potentially Differentiated Profile in AA

- **Durable hair regrowth observed supports potential for transformative paradigm**
  - Mean SALT scores continued to improve from Week 24 to Week 36
  - Multiple reports received of post 36-week hair growth; data collection underway
  - Long term remittive response post-dosing cessation potential supported by literature
- **Response observed across hard-to-treat populations**
  - Responses in both severe (SALT 50-95) and very severe (SALT 95-100) patients
  - Responses in patients with long duration of episodes
    - Mean duration of current episode in SIGNAL-AA Phase 2a was 5-6 years vs 2.5-4 years in prior JAK trials[1,2,3]
    - Literature shows response rates can be half (or less) in patients with current episode >4 years[4,5]
- **Safety profile supports competitive positioning**
  - Potential to drive more patients to treatment, including those ineligible or refusing treatment due to black box safety issues with JAKs

Data supports significant potential opportunity in AA based on efficacy and safety profile;
Part B to support design of and advancement to pivotal trials

[1]King, B. Br J Dermatol 2023; 189:666–673, [2]https://labeling.pfizer.com/ShowLabeling.aspx?id=19638, [3] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/217900s000lbl.pdf, [4]Peeva E, et al. AAD 2019, S034 Late-breaking Research: Clinical Trials Sponsored by Pfizer, [5]King B. World Congress of Dermatology 2023. Sponsored by Eli Lilly and Company

SIGNAL-AA Phase 2a: Part A Complete Through Week 36 Follow-up Period With Ongoing Expansion for Additional Follow-up



Design Elements

Part A

- First exposure in AA patients
- Severe/Very Severe (SALT 50-100)
- No loading regimen
- Dosing: 24-weeks
- Follow-up: 36-weeks

Part B

- Severe/Very Severe (SALT 50-100)
- Introduces loading regimen: designed to accelerate PK/PD dynamics to maximize efficacy
- Longer dosing: 36-weeks
- Longer follow-up: 52-weeks

SIGNAL-AA to characterize profile differentiation vs. currently approved AA agents including JAKs

AA Has Life-Altering Impact and Limited Treatment Options Including JAK Inhibitors Carrying Black Box Warnings

700K[1] people living with AA in the U.S.

Often manifesting **before age 50**

Psychosocially debilitating; scalp and face commonly impacted

Up to **40% become chronic**, including complete loss of scalp[4] and/or body hair[5]

Severity of disease and long duration of episode each associated with more gradual and **lower rates of treatment response**

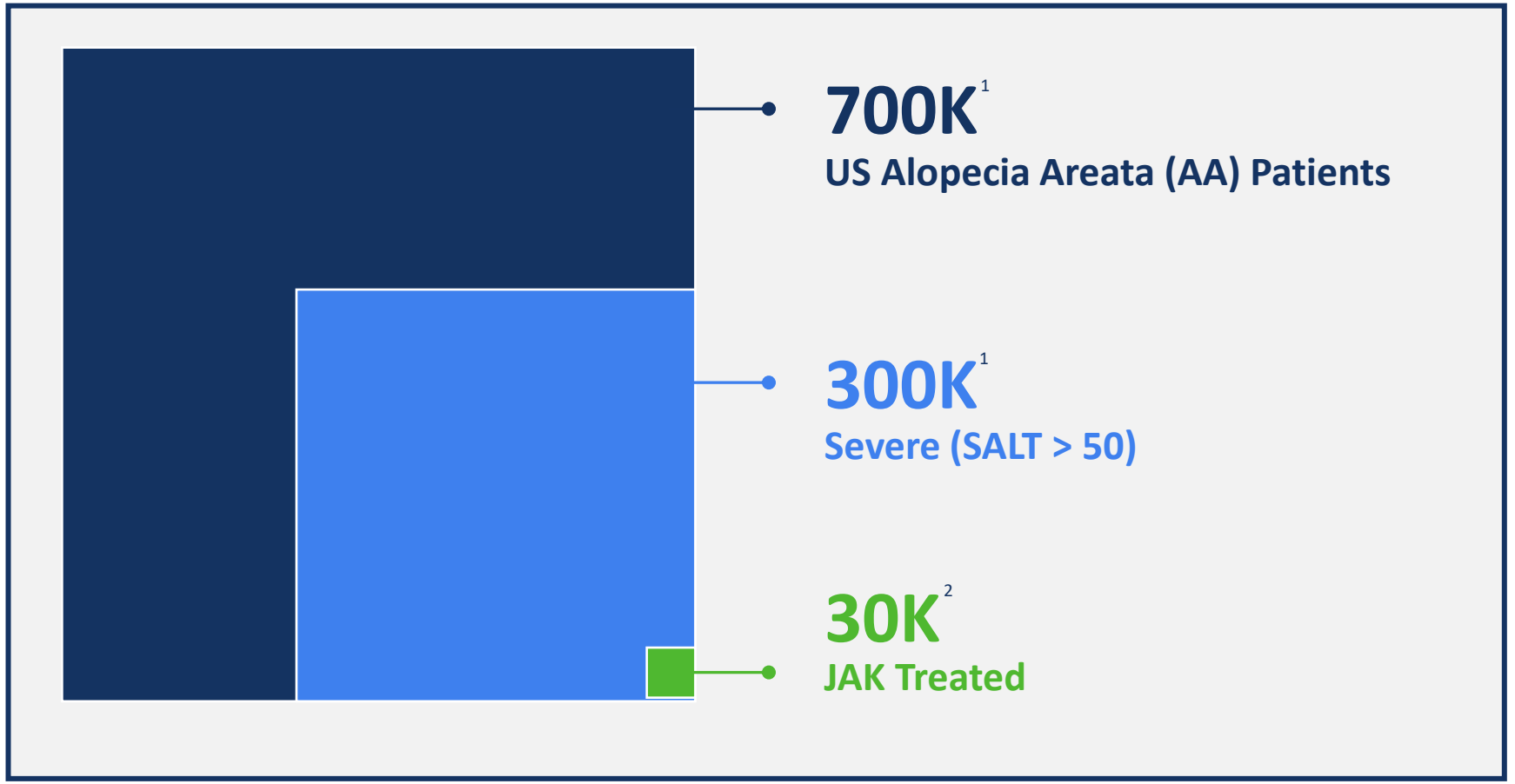
Doctors and patients seek alternatives to currently approved agents[2] including **JAK inhibitors which carry significant safety risks**:

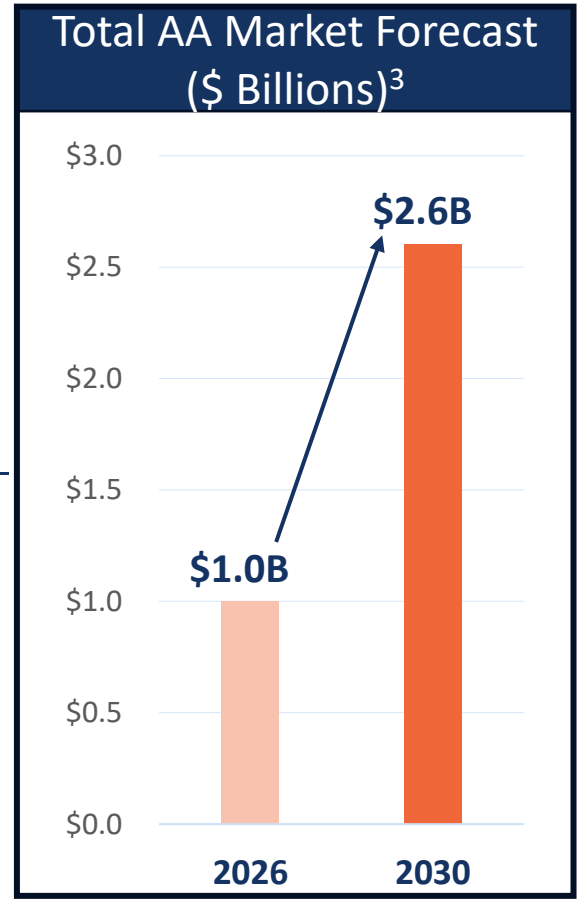
- While they have shown efficacy, they are also associated with **significant adverse events**
- They **require chronic treatment** and **hair loss reoccurs with treatment cessation or taper**
- Olumiant approved in 2022, Litfulo approved in 2023: both carry **class-wide Black Box Warning**[3]

Currently available AA treatment options lack desired profile:
Providers and patients seek safer alternatives
Durable, long-term remission would be transformative

[1]Benigno M, et al. Clin Cosmet Investig Dermatol. 2020 Apr 1;13:259–266, [2]Source: Wells Fargo Research, "Takeaways from Our Investor Lunch with Management and Alopecia Areata KOL" Oct 31, 2024, [3]https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/207924s006lbl.pdf, https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215830s000lbl.pdf, [4]Alopecia Totalis; [5]Alopecia Universalis

AA is Prevalent, Stigmatizing and Psychologically Burdensome; Unmet Need for New Options with Better Safety and Ability to Provide Durable, Long-Term Remittance





[1]Benigno M, et al. Clin Cosmet Investig Dermatol. 2020 Apr 1;13:259–266, [2]Company research; Trinity Life Sciences, [3]Consensus sales forecasts; source: Evaluate Pharma, Jan 2025

A Product With Remittive Properties Could Transform the AA Treatment Paradigm: Potential to Differentiate on Safety and Inducing Long-Term Durable Remission

[T]he potential to have a side effect profile perhaps closer to biologics we use in atopic dermatitis…is certainly a compelling value proposition.

[Patients] would prefer an injection if it was safer in the end.

If it has pristine safety, even with lesser efficacy…it could be used first line.

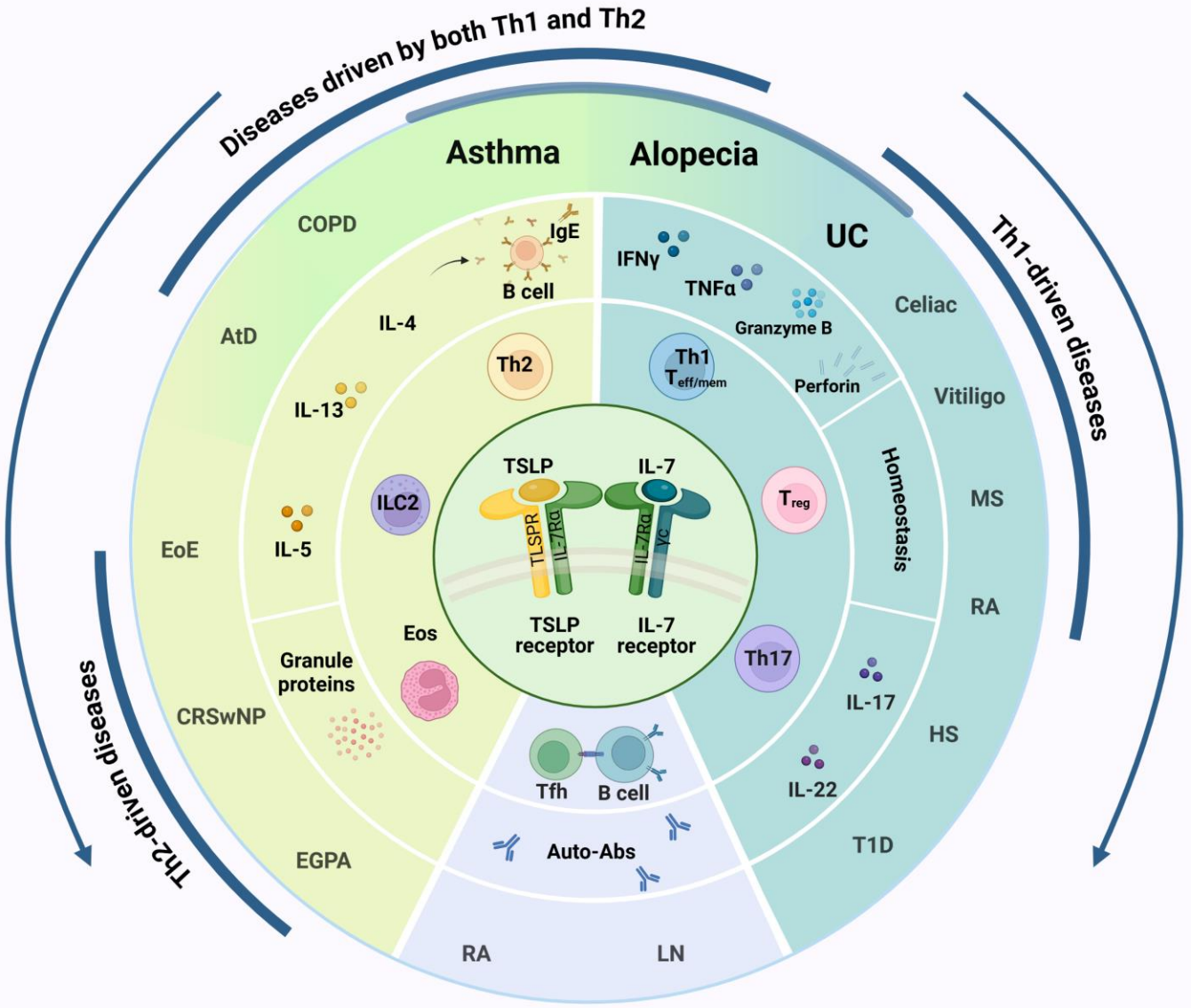
– Excerpts from third party Guidepoint KOL call reviewing Bempkibart Phase 2a data, Dec 12, 2024

Opportunities Beyond AA:
Potential to Expand into a Broad Range of Th1 and Th2 Mediated Diseases

SIGNAL Phase 2a

Meaningful effect on Th2 biomarkers observed

Eosiniphils, IgE, TARC



SIGNAL Phase 2a

Results support the potential for long term, durable responses

Suggestive of T_{eff}/T_{mem} impact

Tissue-Targeted Complement Platform

Lead Asset: ADX-097

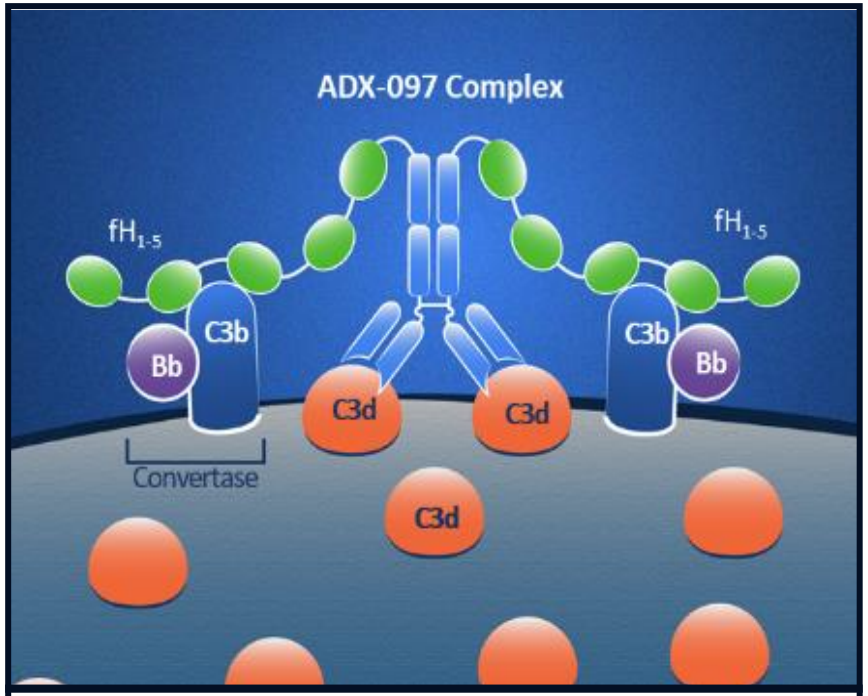
Q32 Tissue-targeted Platform Value Proposition: Designed to Enable Clinical Profile Superior to Systemic Complement Inhibitors

The Unmet Need	The Opportunity
• **Limited activity:** Reliant on systemic blockade for impact on affected organ	• **Enhanced activity through tissue targeting:** Differentiated approach to driving efficacy by inactivating convertases directly at site of destruction
• **High doses, frequent administration required:** High abundance, rapid turnover of most target complement proteins	• **Reduced treatment burden**: SC route with QW dosing; potential for Q2W
• **Infection risk:** Complement plays critical role in combating infection; systemic blockade increases risk	• **Improved risk/benefit profile**: Designed to maximize therapeutic index while maintaining intact immune surveillance; broader indication potential

ADX-097 Lead Bivalent Fusion Protein: Designed with Unique MOA to Drive Localized, Complement Re-regulation for Enhanced Activity and Tolerability

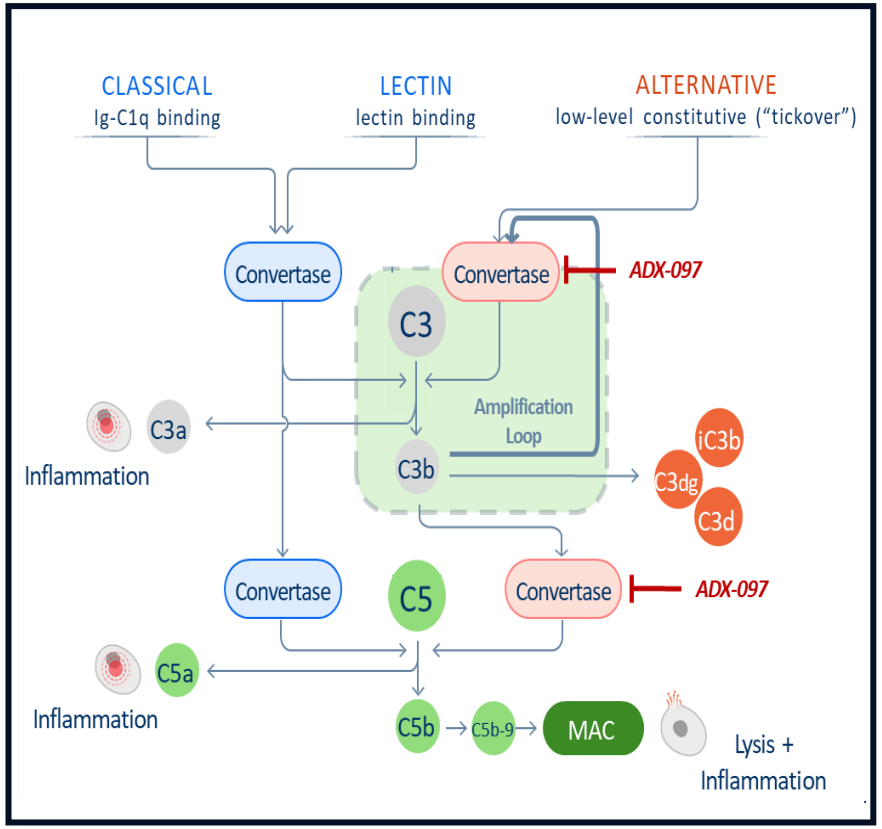
ADX-097 Design: C3d antibody – fH_{1-5}

Designed to be held at site of tissue complement activity allowing catalytic degradation of alternative pathway convertases



ADX-097: Fusion protein
Humanized anti-C3d mAb linked to two moieties of a negative regulatory protein (fH_{1-5})

Inactivation of alternative pathway convertases gains control of amplification loop and all 3 complement pathways



Phase 1 Study:
Complete with Primary Goals Achieved

Phase 1 SAD/MAD (n= 56 Healthy Volunteers)

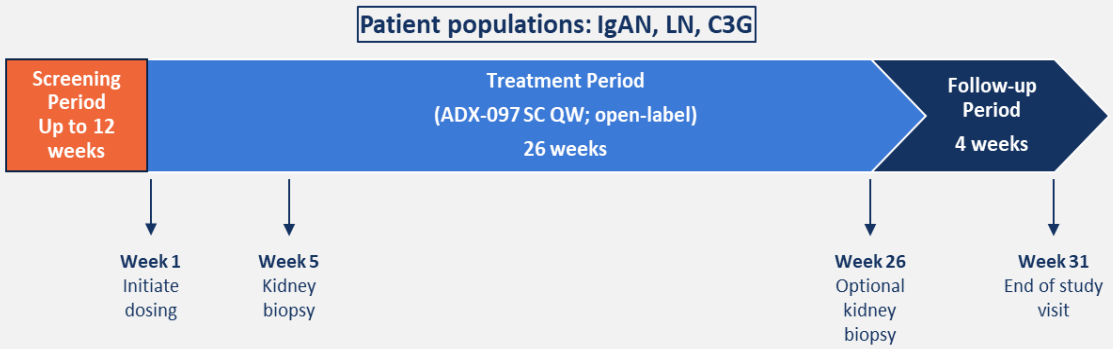
Explored Single Doses of 0.1 - 30 mg/kg IV and/or SC and 450 mg SC Multiple Dose Cohort (~6 mg/kg)

Primary Goals	Achieved	Results
Confirm planned Phase 2 dose/route/schedule	✓	• Attained expected dose-dependent PK/PD • Once weekly SC dosing provided desired exposure for predicted complete tissue inhibition with no concomitant systemic inhibition
Evaluate proximal POM to establish *in-vivo* ADX-097 integrity	✓	• PK levels aligned with predicted Wieslab alternative pathway inhibition
Characterize safety profile	✓	• No serious or severe AEs or discontinuations due to AEs
Characterize immunogenicity risk	✓	• No AEs related to immunogenicity • Minimal anti-drug antibodies (ADA) detected across SAD/MAD; low level titers

ADX-097 SPOTLIGHT Phase 2 Renal Basket Clinical Trial: Enrollment Ongoing

Details and Timeline

Renal Basket (n= up to 30)
26-week treatment



- Open-label trial designed to assess safety, tissue pharmacology and magnitude/timing of treatment effect
- Key assessments: Drug localization and impact in tissue, biomarkers (including proteinuria and eGFR) for assessment of ADX-097 activity
- Anticipated to provide data for key regulatory discussions

Trial initiated; topline results expected in 2H'25, with initial open-label data by 1H'25

ADX-097: Significant Market Opportunity

Significant Market Opportunity including in Initial Focus on Renal Diseases (LN, IgAN, C3G)

Lupus Nephritis (LN)

- **6-fold mortality risk** increase vs general population[1,2]
- Up to 30% develop **kidney failure** requiring dialysis or kidney transplant **within 15 years of diagnosis**[3,4]

IgA Nephropathy (IgAN)

- **Up to 40%** develop ESRD w/in 20 years of diagnosis[5,6], and patients have **10 years** reduced life expectancy[7,8]
- **~70% not adequately controlled** w/supportive care[5,9]

C3 glomerulopathy (C3G)

- **Up to 50% of adult, 70% of pediatric** patients progress to **kidney failure** within 10 years[10-13]
- **>70%** experience **recurring disease**; ~50% experience allograft loss w/in 10 years of kidney transplant[10,14-17]

[1] Watts et al. Nat Rev Rheum 2022; [2] Estimated using U.S. and Norway incidence study results, and Norway prevalence study results as applied to U.S. population; [3] Hoover et al. Kidney Int 2016; [4]Pryor et al. Rheum Dis Clin North Am. 2021; [5] Kwon et al. J Health Econ Outcomes Res. 2021; [6] Swaminathan et al. Clin J Am Soc Nephrol 2006; [7]Bomback et al. Kidney Int. 2018. [8]Smith et al. Natur Rev Nephrol. 2019; [9]Servais et al. Kidney Int 2012; [10]Ronco et al. Nat Rev Dis Primers 2021; [11] Swaminathan et al. Clin J Am Soc Nephrol 2006; [12] Hanko et al. Nephrol Dial Transplant 2009;; [13]Umehara et al. Mod Rheum 2012; [14] Uchida et al. Int J Rheum 2012; [15] Estimated using Japan prevalence study results as applied to U.S. population; [16] Based on 2020 Census population

[1]Mahajan et al. Lupus 2020; [2]Cervera et al. Medicine 2002; [3]Maroz et al. Am J Med Sci 2013. [4]Ward et al. J Rheumatol 2009; [5]Habas et al. Medicine (Baltimore) 2022. [6]Berthoux et al. Semin Nephrol 2008; [7]Pitcher et al. Clin Jour of Amer Soc Neph 2023. [8] Hastings et al. Kidney Int Rep 2018; [9]Raun et al. N Engl J Med 2015; [10]Heiderscheit et al. Am J Med Genet C Semin Med Genet 2022. [11]Smith et al. J Am Soc Nephrol 2007; [12]Servais et al. Kidney Int 2012; [13]Rabasco et al. Kidney Int 2015; [14]Smith et al. Nat Rev Nephrol 2019. [15]Welte et al. BMC Nephrology 2018; [16]Salvadori et al. WJT 2016. [17]Regunathan-Shenk et al. AJKD 2019 [18]Hoover et al. Kidney Int 2016; [19]. Pryor et al. Rheum Dis Clin North Am. 2021; [20]. Braun et al. Int Urol Nephrol 2011; [21] McQuarry et al. Kidney Int 2013; [22] Bomback et al. Kidney Int. 2018.

Summary:
Financial Overview and Anticipated Milestones

Q32 Bio Has Significant Potential to Unlock Near-term Value Creation

Runway through multiple Phase 2 clinical readouts and into mid-2026

Financial Overview

- Q3 cash balance of $89.1M, providing expected cash runway **to mid 2026**
- Approximately 12.1M shares outstanding

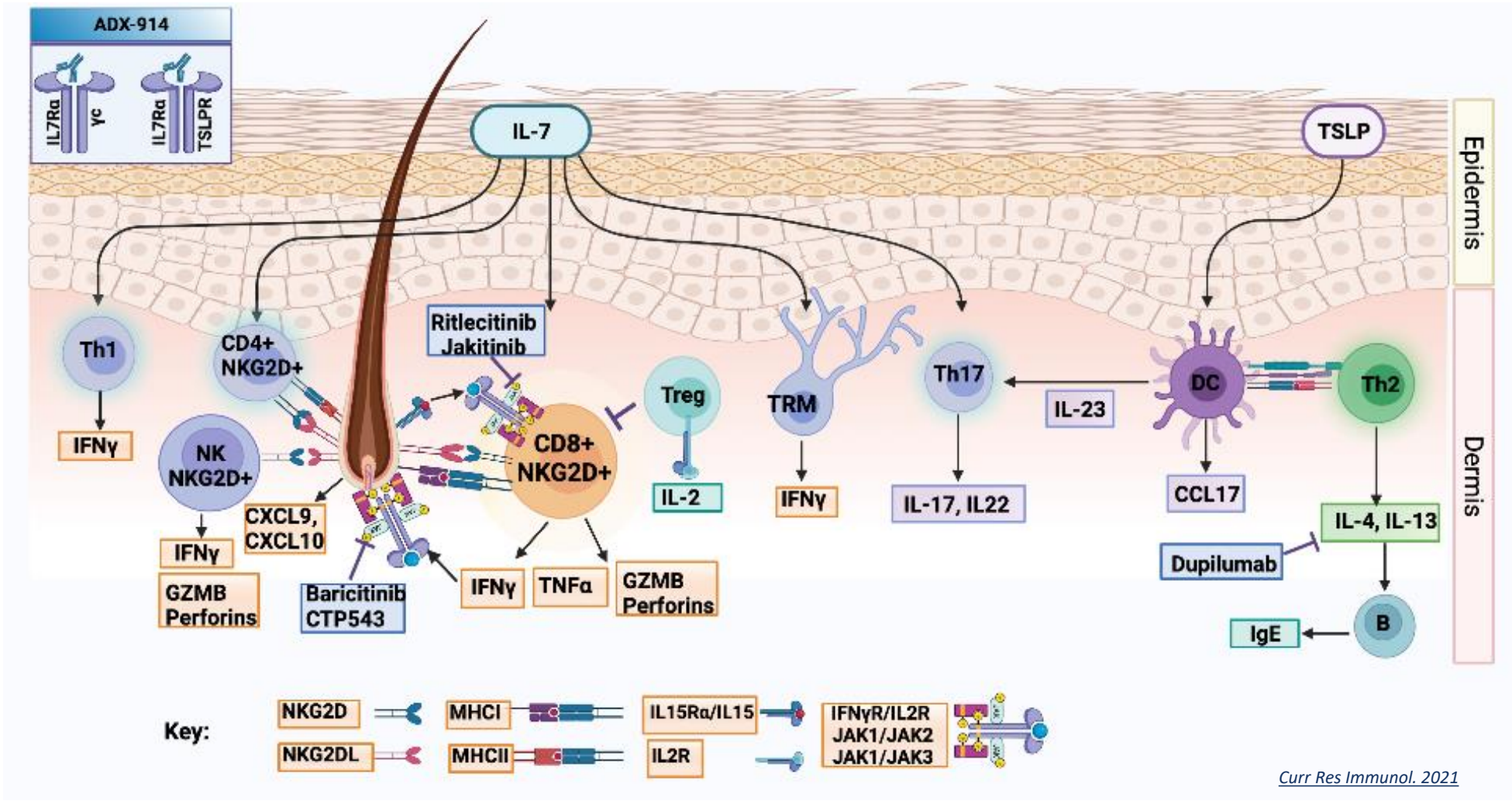
Numerous Anticipated Milestones

- **1H'25 – Bempikibart:** Initiate enrollment in SIGNAL-AA Phase 2a Part B
- **1H'26 – Bempikibart:** SIGNAL-AA Phase 2a Part B Topline results
- **1H'25 – ADX-097:** Renal basket Phase 2 Initial data
- **2H'25 – ADX-097:** Renal basket Phase 2 Topline results

APPENDIX

Bempikibart in AA: IL-7 Inhibition is Believed to Block CD8+ T cell-Driven Inflammation

Hair Follicle Immune Dysregulation in Alopecia



Curr Res Immunol. 2021

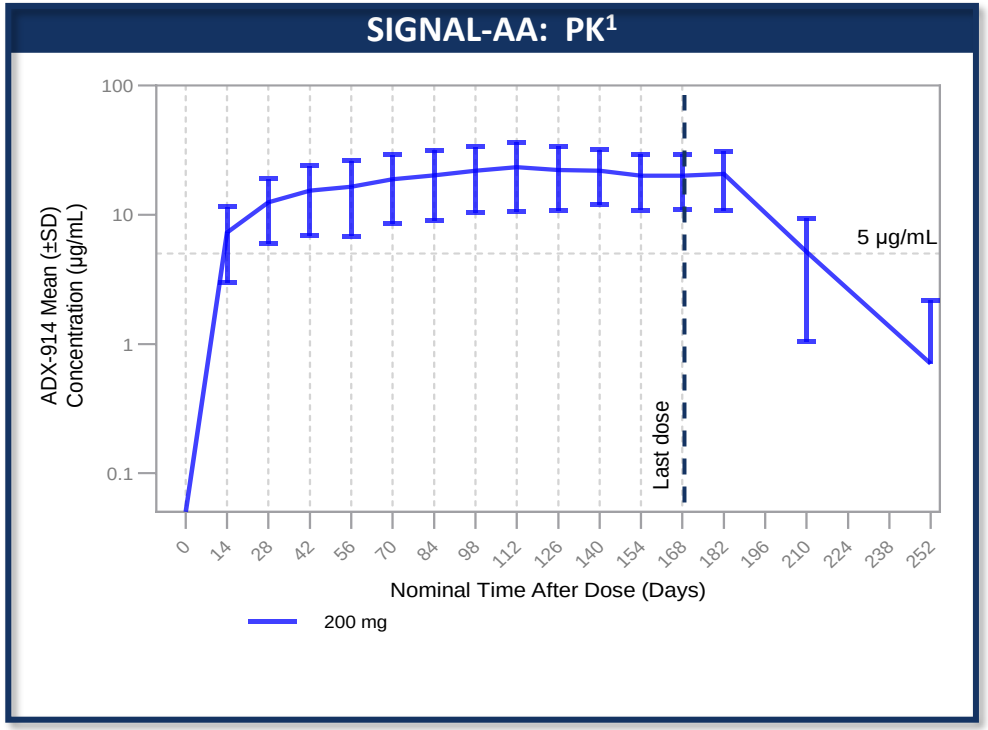
Bempikibart Shows Potential to be Best in Class IL-7Rα Antibody

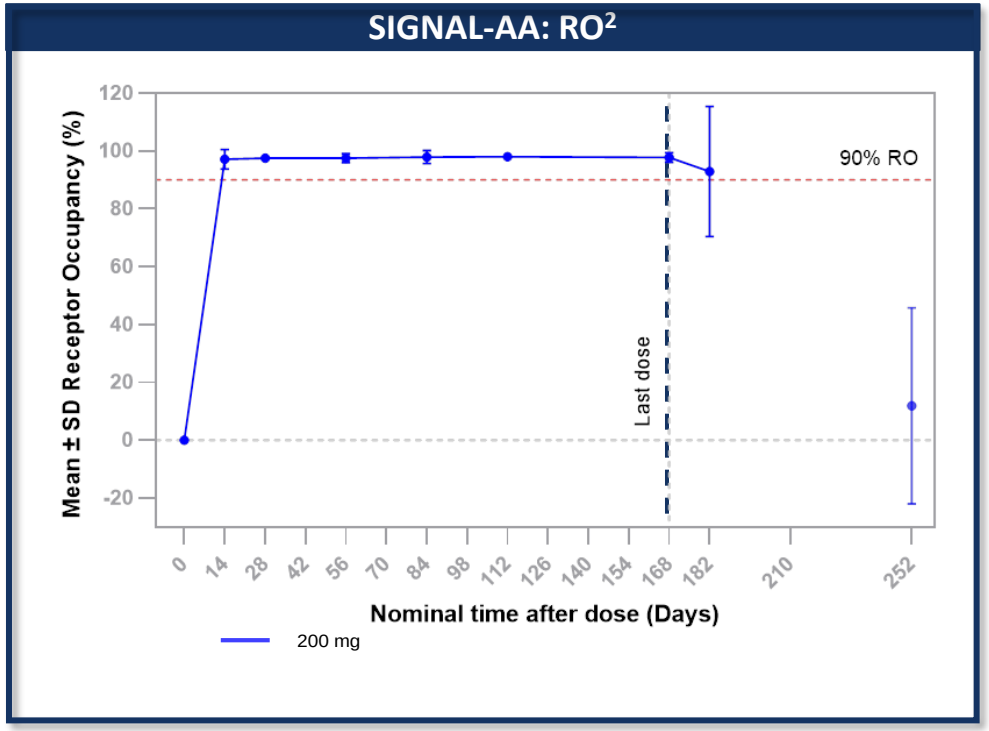
	Bempikibart **Q32 Bio** (IgG1 Effector-less)	**Lusvertikimab (OSE-127)** **OSE** (IgG4)	**ZB-168** **Zura Bio (formerly Pfizer)** (IgG1)	**GSK-2618960** **GSK** (IgG1)
Active in development	✓	✓	**Not currently funded[1]**	✗
Antagonist	✓	✓	--	✗
PK/PD supports current single-injection SC formulation	✓	✗	✗	✗
Fully human	✓	✗	✓	✗
Antibody generation	Medarex (fully human)	Rat mAb (humanized)	Phage library	Murine mAb (humanized)
IL-7R binding on cells ($EC_{50,}$ nM)[2]	0.08	0.24	0.04	0.32
IL-7Rα binding affinity, biacore (K_D, nM)[2]	0.09	0.16	0.13	0.23
Inhibition of IL-7 induced pSTAT5 in T-cells (IC_{50} nM)[2]	0.22	0.31	0.37	0.41
Inhibition of TSLP induced signaling in monocytes (IC_{50} nM)[2]	2.88	1.07	0.20	7.47

Bempikibart at 200 mg clinically demonstrated potent IL-7 and TSLP inhibition via changes in Th2 biomarkers and T-cells[3]

[1]Zura Bio, https://investors.zurabio.com/news-events/presentations; development dependent on additional financing and pending topline data from other programs, [,2]Company data; data were generated by Q32 Bio in side-by-side assay of bempikibart vs comparator IL-7Rα mAb analogues, [3]Results from Phase 2a SIGNAL-AA and SIGNAL-AD clinical trials

SIGNAL-AA Part A: Favorable PK and Receptor Occupancy (RO) Achieved





Bempikibart Phase 2a achieved expected PK and RO, supporting current subcutaneous (SC) dosing 200 mg (SC): ≥5 µg/mL mean concentration and >90% RO in 90% of patients, consistent with Phase 1 results

[1]Excludes samples impacted by missed dose (PK), [2]Excludes samples impacted by missed dose or assay deviation (RO)

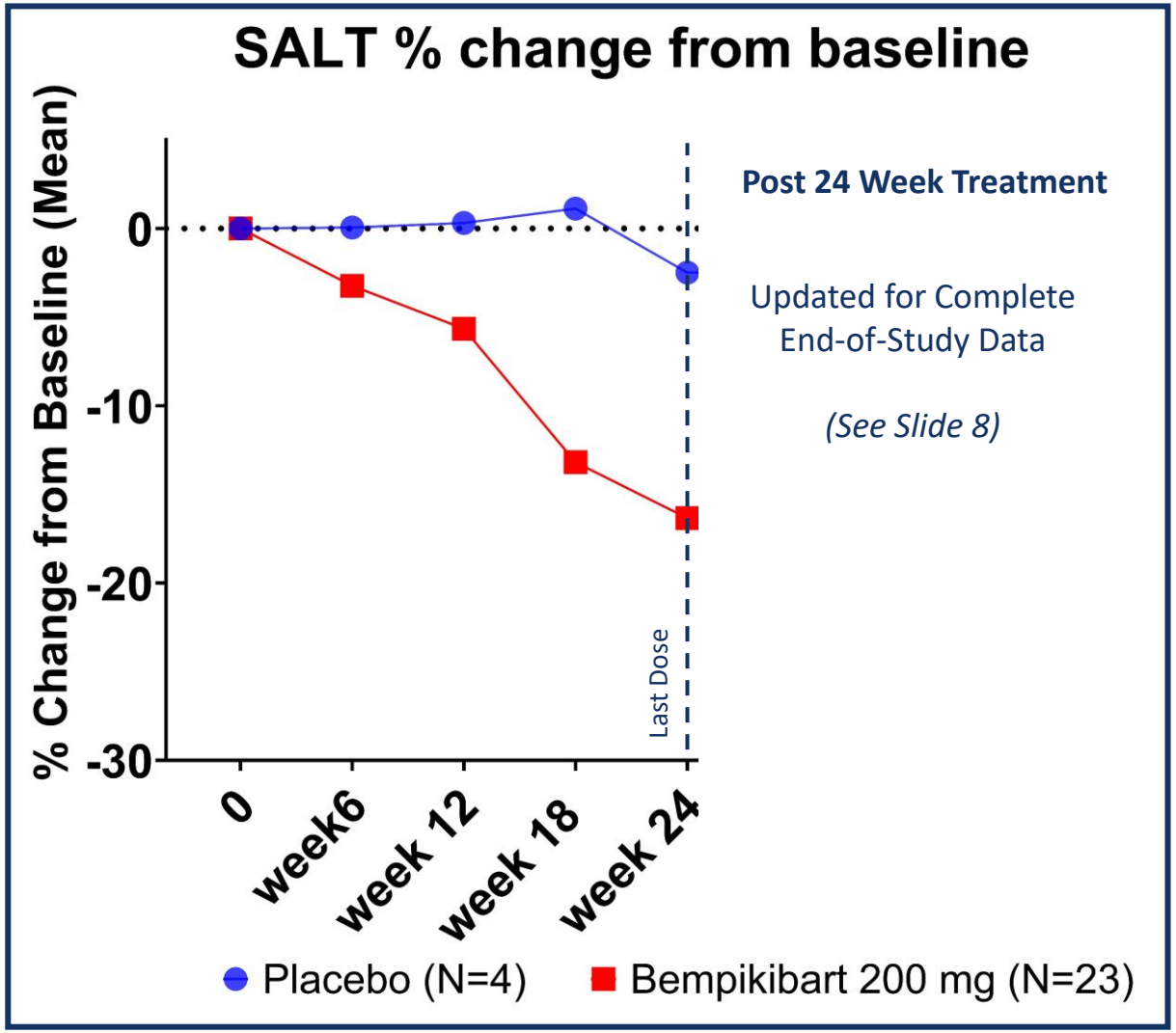
SIGNAL-AA Part A: Baseline Characteristics

mITT (n=44)		
	Bempikibart 200 mg (n=33)	Placebo (n=11)
Gender (n, %)	Female (27, 81.8%)	Female (7, 63.6%)
Age (years, Mean ± SD)	48.8 ± 10.2	47.1 ± 14.2
Race (n, %)	White (19, 57.6%) Black /African American (10, 30.3%) American Indian/Alaska Native (1, 3.0%) Asian (1, 3.0%) Missing (2, 6.0%)	White (4, 36.4%) Black/African American (6, 54.5%) Asian (1, 9.1%)
Body weight (kg, Mean ± SD)	82.7 ± 13.9	85.1 ± 16.9
Baseline SALT Scores (Mean ± SD)	75.0 ± 20.3	75.5 ± 21.6
Duration of current episode (months, Mean ± SD)	68.5 ± 36.2	51.7 ± 36.5

Revised Per Protocol[1] (n=27)		
	Bempikibart 200 mg (n=23)	Placebo (n=4)
Gender (n, %)	Female (18, 78.3%)	Female (2, 50.0%)
Age (years, Mean ± SD)	47.7 ± 11.3	59.8 ± 11.9
Race (n, %)	White (14, 60.9%) Black/African American (7, 30.4%) Other (2, 8.7%)	White (3, 75.0%) Black/African American (1, 25.0%)
Body weight (kg, Mean ± SD)	81.9 ± 14.2	82.3 ± 12.2
Baseline SALT Scores (Mean ± SD)	75.4 ± 20.7	88.4 ± 22.5
Duration of current episode (months, Mean ± SD)	58 ± 37.2	36.5 ± 21.2

[1] Table reflects Revised Per-Protocol Population (defined as pre-specified per-protocol population removing 3 placebo patients from one site excluded for marked protocol violations of entry criteria)

SIGNAL-AA: Topline Data, as Presented December 10, 2024



Post 24 Week Treatment

Updated for Complete End-of-Study Data

(See Slide 8)

Figure reflects Revised Per-Protocol Population

KEY FINDINGS:

Clinical Activity Observed in SIGNAL-AA

- Mean change in SALT 16% vs 2% for placebo (Week 24)
- Mean change in SALT 18% vs 2% for placebo (Week 26)
- SALT-20 achieved in 9% at Week 24, 13% at Week 26

Activity Observed Despite Difficult to Treat Population

- Mean duration of current episode 58 months (~5 yrs)
- Duration of current episode (>4 yrs) associated with more gradual responders, late responders, and lower percentage of patients achieving SALT-20[1]

[1]King, B World Congress of Dermatology 2023

SIGNAL Phase 2a: Favorable Safety and Tolerability Profile in Phase 2a with No Grade 3 or Higher Related AEs

Adverse Events (SIGNAL Trials Through Week 24)

	Bempikibart 200 mg (N=96) n (%) [E]	Placebo (N=69) n (%) [E]
Participants with at least one TEAE	55 (57.2) [154]	30 (43.5) [76]
Participants with at least one TEAE by greatest reported relationship with study treatment [a]		
Not related	28 (29.2) [43]	23 (33.3) [47]
Related	27 (28.1) [68]	7 (10.1) [12]
Participants with at least one TEAE by worst reported severity CTCAE grade [b]		
Grade 1 - Mild	30 (31.2) [49]	13 (18.8) [27]
Grade 2 - Moderate	20 (20.8) [21]	15 (21.7) [22]
Grade 3 - Severe[1]	4 (4.1) [6]	2(2.9) [2]
Grade 4 - Life threatening [2]	1 (1) [1]	0 [0]
Grade 5 - Death	0 [0]	0 [0]

Well-tolerated safety profile

Findings consistent through AA Week 36[3]

Low incidence of infections, low incidence of lymphocyte decreases (≤Grade 2)

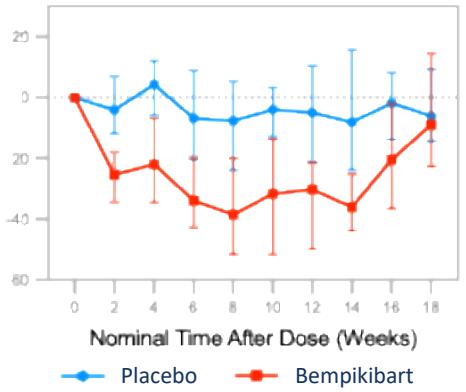
[1]Bempi arm (all not related): Acute myocardial infraction, supraventricular tachycardia, acute respiratory failure, bone fracture, CPK increase, Coronary Artery Stenosis LAD [2] anaphylactric reaction (nut allergy), [3] Only 3 additional non-infection/non-lymphocyte AEs reported in 2 subjects through week 36; n=1 placebo/n=2 treated (all mild)

Substantial Activity on Biomarkers Observed in Clinical Trials Supports Potent Inhibition of TSLP and IL-7 Mediated Signaling

Th2 Biomarkers: SIGNAL Phase 2a[1]

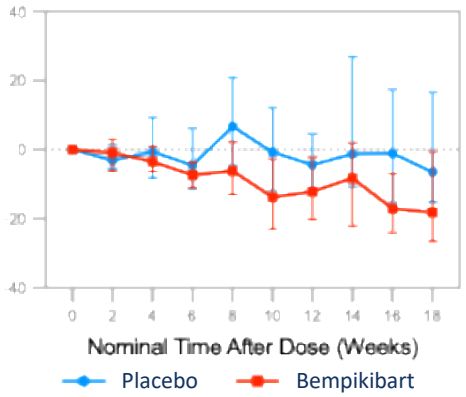
Median Changes Over Time (95% CI)

TARC



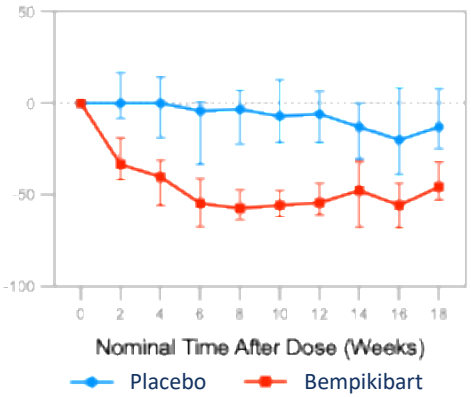
TARC decrease up to 39%

IgE



IgE decrease up to 18%

Eosinophils



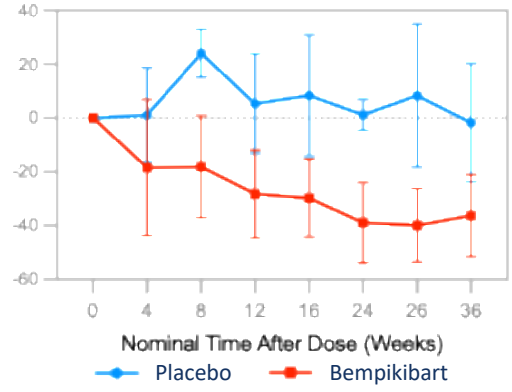
Eos decrease up to 57%

TARC and eosinophil changes significant at multiple time points ($p < .05$)

Th1 Biomarkers: SIGNAL Phase 2a[2]

Mean Changes Over Time (±SD)

CD3⁺ T cells



CD3⁺ T cell decrease up to 40%

CD3⁺ changes significant at multiple time points ($p < .05$)

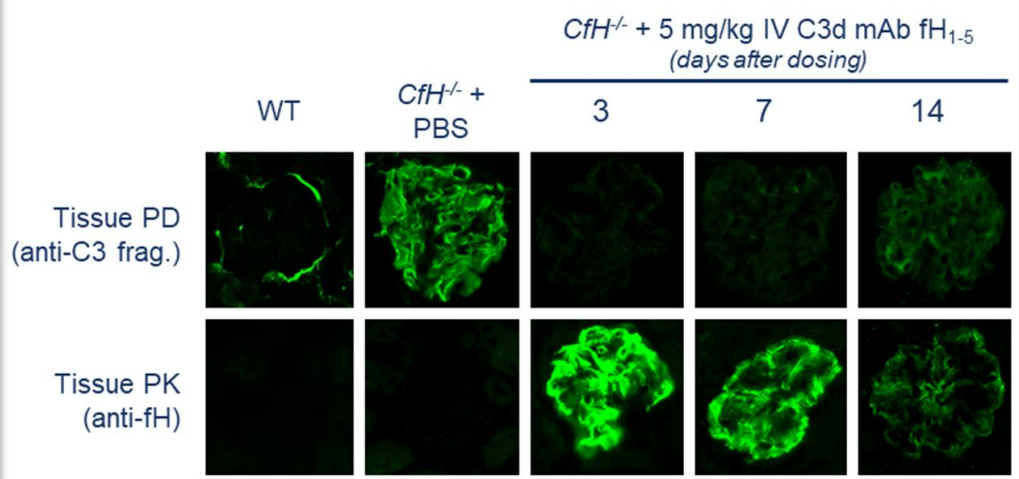
Figures depict biomarkers for all enrolled patients in SIGNAL-AD and SIGNAL-AA except samples impacted by missed dose; Patients treated for 12 weeks in SIGNAL-AD, 24 weeks in SIGNAL-AA. [1] Results from SIGNAL-AD and up to Nov 5th, 2024; [2]Results from SIGNAL-AA and up to Dec 10th, 2024.

ADX-097 Preclinical Data: Desired PK/PD, Favorable Tolerability and Immunogenicity

Preclinical data supports ADX-097 as a tissue-targeted complement inhibitor

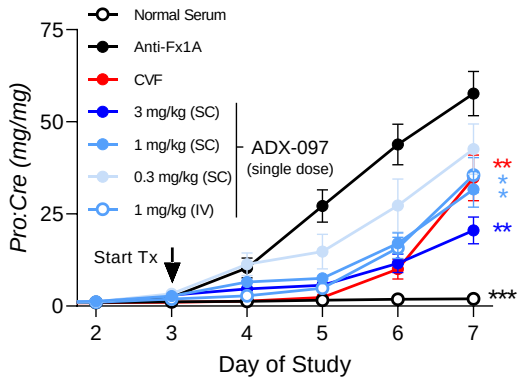
- Durable (>7 days) tissue PK/PD after SC dosing
- Reduction in key proof of mechanism/proof of concept biomarkers including proteinuria and sC5b
- Over 40x safety margin for planned Phase 2 clinical dosing

Potent Tissue PK/PD in *CfH*$^{-/-}$ Mice



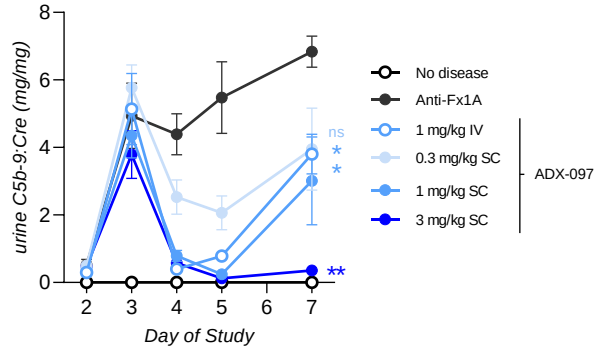
Robust Effect on POM/POC Endpoints in Rat PHN[1] Model

Proteinuria



Potent inhibition equivalent to full systemic complement depletion

Urine sC5b-9



Potent inhibition of urine sC5b-9, a non-invasive approach to monitor complement inhibition in kidney

[1]Passive Heymann Nephritis