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Three unique dual-pathway biologics, clinically validated for therapeutic areas with unmet needs

August 2024

Nasdaq Ticker: ZURA

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Company Summary

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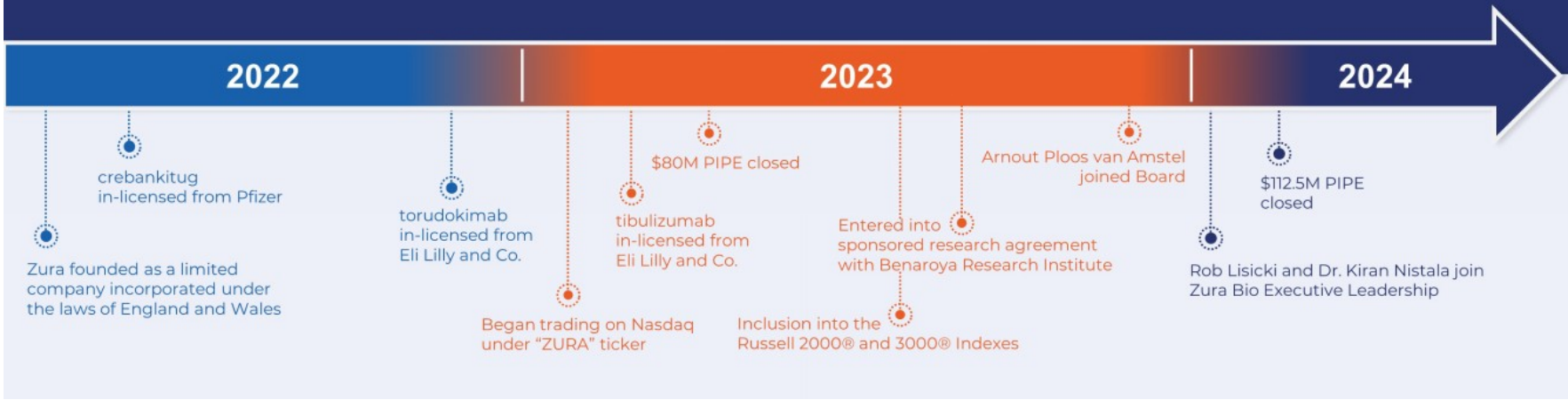
High-Potential Biologics: Three novel, clinically validated dual-pathway biologics, each with multi-billion-dollar potential, ready for Phase 2.

Lead Asset Development: Phase 2 study for tibulizumab targeting SSc starts in 4Q 2024, followed by HS in 2Q 2025.

Strategic Milestones: Expecting 2 internal catalysts and up to 11 external readouts over the next 36 months, driving value creation.

Proven Leadership: Experienced team with a strong track record in autoimmune drug development and commercialization.

Financial Strength: Cash runway through 2027.



Pipeline of novel dual-pathway biology clinical stage assets potentially offers broader and improved clinical responses

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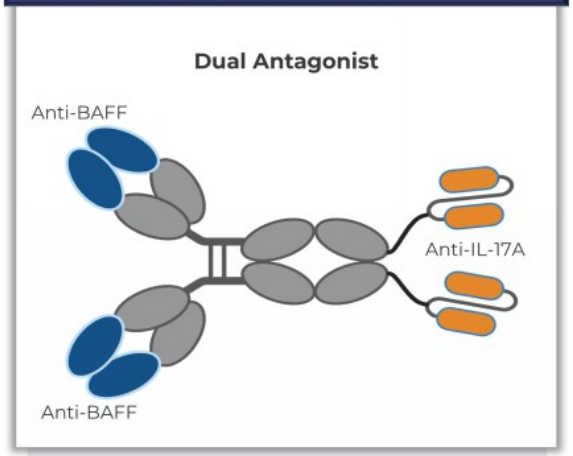
tibulizumab
ZB-106

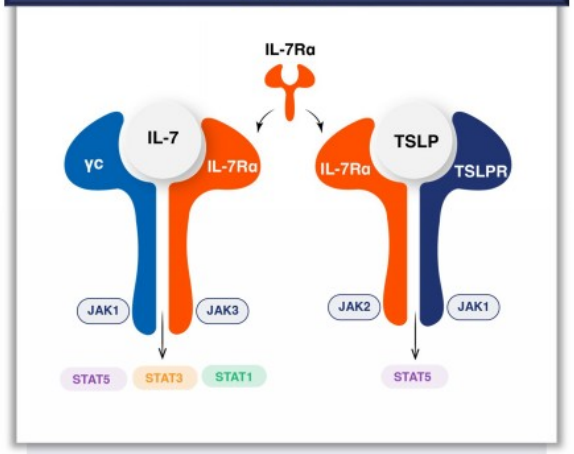


78 Participants Dosed Across Three Ph 1/1b studies

57 participants with single dose

21 participants with multiple doses up to 12 weeks

crebankitug
ZB-168

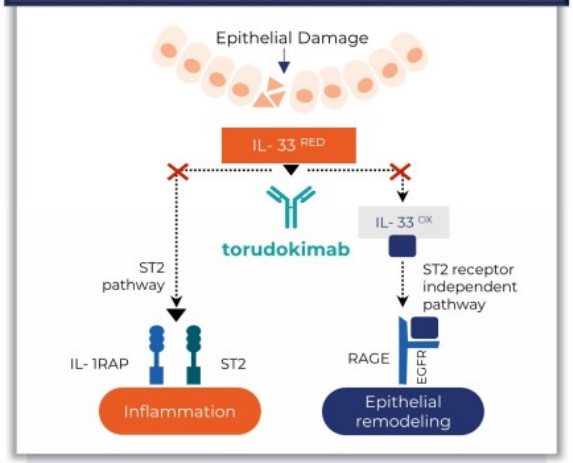


93 Participants Dosed

60 participants with single dose

33 participants with multiple doses up to 12 weeks

torudokimab
ZB-880



244 Participants Dosed

81 participants with single dose

163 participants with multiple doses up to 52 weeks

(*) includes data from trials run by Pfizer and Eli Lilly
Sources: Zura CSRs and Internal Data
Acronyms: BAFF, B cell-activating factor; EGFR, epidermal growth factor receptor; JAK, janus tyrosine kinase; IL, interleukin; RAGE, receptor for advanced glycation end products; ST2, growth STimulation expressed gene 2; TSLP, thymic stromal lymphopoietin

Zura is led by a strong leadership team with a successful track record in drug and business development

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and Director

VERENDER BADIAL
Chief Financial Officer

KIRAN NISTALA M.B.B.S., Ph.D.
Chief Medical Officer and
Head of Development

GARY WHALE Ph.D.
Chief Technology Officer

KIM DAVIS J.D.
Chief Legal Officer

MICHAEL HOWELL Ph.D.
Chief Scientific Officer and
Head of Translational Medicine

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Key Anticipated Events through 2026

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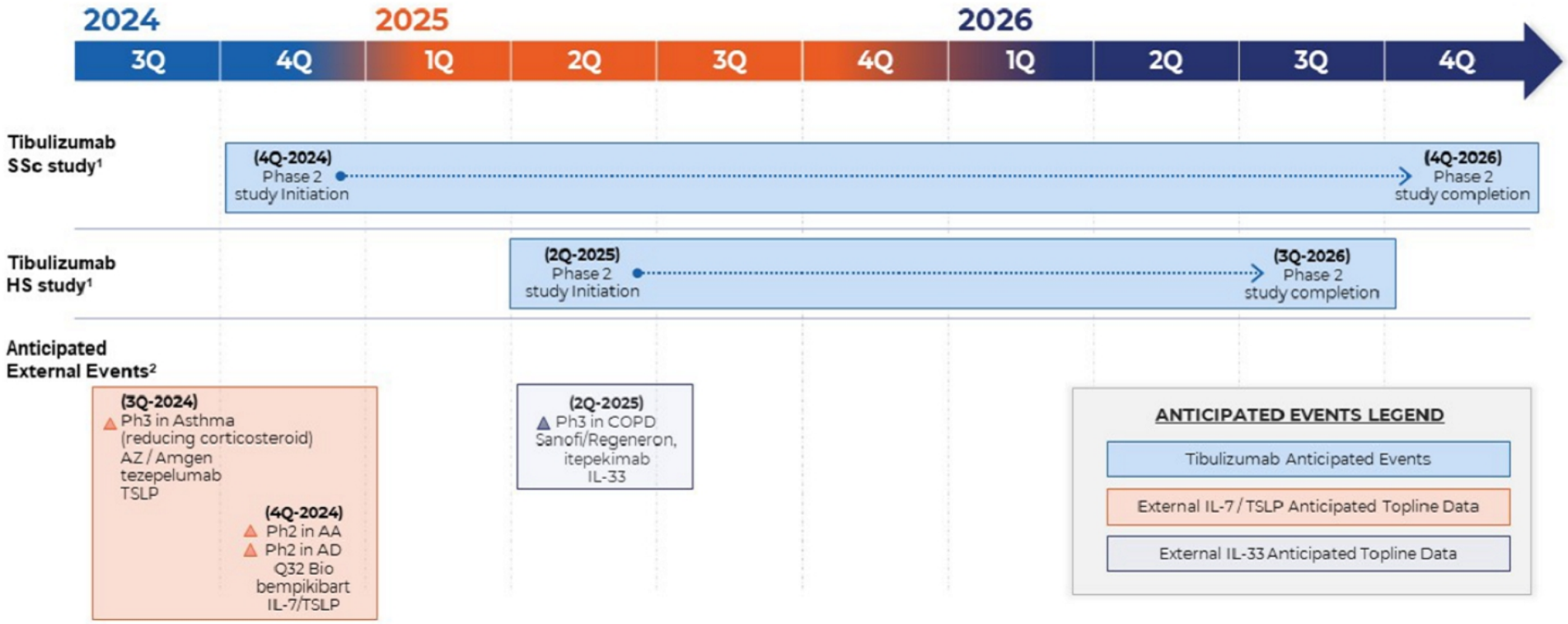

Sources: [1] Zura Planning Assumptions, [2] clinicaltrials.gov, Company Presentations

Acronyms: AA, alopecia areata; AD, atopic dermatitis; COPD, chronic obstructive pulmonary disease; CRO, contract research organization; FDA, Food and Drug Administration; HS, hidradenitis suppurativa; IL, interleukin; SSc, systemic sclerosis; TLD, topline data; TSLP, thymic stromal lymphopoietin; UC, ulcerative colitis

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Key Highlights for tibulizumab in systemic sclerosis

Tibulizumab offers a *dual-pathway approach* and potentially *paradigm changing* therapy to SSc patients, if approved

- IL-17 and BAFF are upregulated in SSc, and present in serum and skin of SSc patients
- **In separate studies, brodalumab [IL-17] and belimumab [BAFF] have demonstrated clinically relevant biological effects in lung & skin in phase 2 and phase 3 studies [1,2]**
- Tibulizumab's dual-pathway biology combines IL-17 + BAFF pathways, offering potential as a pioneering first-in-class therapy
- Tibulizumab may offer the convenience of Q4W SC dosing

Sources: [1] Fukasawa, T., et al. Annals of the Rheumatic Diseases, doi:10.1136/annrheumdis-2022-eular.2519.
[2] Gordon, Jessica K., et al. Arthritis Rheumatology, doi:10.1002/art.40358.

Acronyms: BAFF, B cell-activating factor; IL, interleukin; Q4W, every four weeks; SSc, systemic sclerosis; SC, subcutaneous

Tibulizumab is designed to target the combination of two clinically validated pathways for SSc

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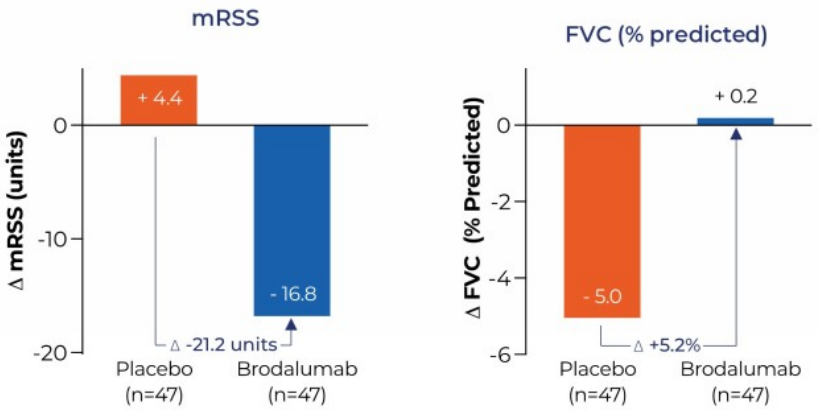
Brodalumab

IL-17 receptor antagonist

- Achieved 1° endpoint of treatment difference of least square mean: (−21.2 [95% CI -3.9, -18.5]; P<0.001), in mRSS and 2° endpoint of improved FVC, both at 24 weeks [1]
- Demonstrated therapeutic effects on lung/respiratory functions, digital ulcers, the symptoms of gastroesophageal reflux disease, and QOL without noteworthy safety concerns

CLINICAL PRECEDENT

Phase 3 brodalumab study (24 weeks)



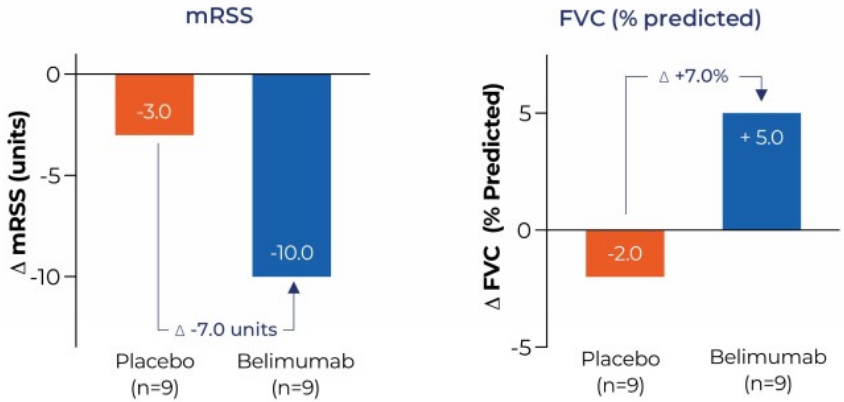
Belimumab

BAFF antagonist

- 52-week, investigator initiated, single center, double blind, placebo-controlled pilot study in 20 participants with dcSSc on MMF [2]
- Both treatment groups experienced improvements in mRSS favoring belimumab (-10 vs -3; p=NS)
- Secondary endpoints were met with statistical significance in two endpoints: SHAQ-DI and VAS Raynaud's phenomenon

CLINICAL PRECEDENT

Phase 2 belimumab IIT study (52 weeks)



Sources: [1] Fukasawa, T., et al. Annals of the Rheumatic Diseases, doi:10.1136/annrheumdis-2022-eular.2519. [2] Gordon, Jessica K., et al. Arthritis Rheumatology, doi:10.1002/art.40358.

Acronyms: BAFF, B cell-activating factor; dcSSc, diffuse cutaneous systemic sclerosis; FVC, forced vital capacity; IIT, investigator-initiated trial; MMF, mycophenolate mofetil; mRSS, modified Rodnan skin score; QOL, quality of life; SHAQ-DI, scleroderma health assessment questionnaire – disability index; SSc, systemic sclerosis; VAS, visual analogue scale

TAM projected at $2B by 2028

Significant unmet need in systemic sclerosis

- **No advanced-line agents currently approved** for skin and lung
- Global prevalence of **200,000 patients with 100,000 SSc patients** in US
- Penetration of advanced line agents projected to **peak at ~35%**
- TAM projected to reach **$2B by 2028**
- SSc forecasted **CAGR of 4.2% (2021 – 2028)**

Sources: Coherent Market Insights: Scleroderma 2022-2028. Global Data: Systemic Sclerosis – Global Drug Forecast and Market Analysis to 2030
Acronyms: CAGR, compound annual growth rate;, SSc, systemic sclerosis; TAM, total addressable market; US, United States

We are developing Tibulizumab as a differentiated treatment for SSc patients

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We are developing tibulizumab to potentially address three critical gaps

01 EFFICACY

Potential for broader and improved clinical effect in skin ***and*** lung in a single therapy

02 TOLERABILITY

The two components of tibulizumab have been safely administered to ~150,000 study participants or patients[1]

03 CONVENIENCE

Designing to avoid onerous monitoring and potentially offer convenient Q4W SC dosing

[1] administered as mono-therapy ixekizumab or mono-therapy tabalumab

Sources: clinicaltrials.gov, Lilly press release, dated 2021, April 30, retrieved from URL , Taltz® delivers more cumulative days with completely clear skin for adults with psoriasis compared to seven other biologics in novel network meta-analysis

Acronyms: HCP, healthcare provider; Q4W, every four weeks; SC, subcutaneous; SSc, systemic sclerosis

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Key Highlights for tibulizumab in hidradenitis suppurativa

Tibulizumab combines *two validated HS mechanisms* into one single therapy

- Scientific validation of the role of IL-17 and B cells in hidradenitis suppurativa
- Multiple positive phase 2 and phase 3 studies in the industry with IL-17 inhibitors or B cell depleting therapies [1]
- Despite new options unmet need remains, PBO adjusted HiSCR75 deltas are in the 20% to 30% range [1]
- Dual-pathway biology combines two clinically validated therapeutic targets into a single agent
- Developing to potentially offer convenient Q4W SC dosing

Sources: [1] Company Presentations, Publications and Research.
Acronyms: HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; IL, interleukin; PBO, placebo, Q4W, every four weeks; SC, subcutaneous

Role of IL-17 and B cells is clinically validated, however clinical effect remains modest with single-pathway inhibition

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Company / Asset*		NOVARTIS COSENTYX®	NOVARTIS remibrutinib*	UCB BIMZELX®	MoonLake sonelokimab	MoonLake sonelokimab	ACELYRIN izokibep	ACELYRIN izokibep	rigel fostamatinib
Mechanism		IL-17 A	BTKi	IL-17 A/F	IL-17 A/F	IL-17 A/F	IL-17 A/A	IL-17 A/A	SYK inhibitor
Administration		SC/IV	PO	SC	SC	SC	SC	SC	PO
Phase		Phase 3	Phase 2b	Phase 2	Phase 2	Phase 2	Phase 2b	Phase 2b	Phase 2
Dosing		30mg Q2W for 16W	100 mg or 25 mg BID	320mg Q2W for 12W	120mg Q2W for 12W	120mg Q2W for 24W	160mg QW for 12W	160 mg Q2W or QW for 12W	150 mg BID for 12W
Total Patients		n = 360	N = 77	n = 88	n = 234	n = 234	n = 30	n = 175	n = 20
Efficacy (HiSCR50)	Non-Placebo Adjusted	42% - 45%	48.5% - 72.7%	63%	66%	76%	71%	42% - 46%	85%
	Placebo Adjusted	11% +	38%	35%	38%	48%	N/A	1% - 5%	N/A
Efficacy (HiSCR75)	Non-Placebo Adjusted	N/A	27.3% - 42.4%	50%	43%	57%	57%	34% - 39%	70%
	Placebo Adjusted	N/A	24%	29%	29%	N/A	N/A	5% - 10%	N/A
Safety	Candidiasis	0% - 3%[1]	0	9%	10.5%	>10%	0%[2]	TBD	0%

(*) There have been no head-to-head clinical trials between the product candidates listed above. Study designs and protocols for each product candidate were different, and as a result, results may not be comparable between product candidates.

Sources: Company Presentations, Publications and Research.

[1] Represents data from psoriasis trial. [2] Represents safety data from psoriatic arthritis trial remibrutinib, 2024 AAD S026.

Acronyms: BID, twice a day; BTKi, Bruton tyrosine kinase inhibitors; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; IL, interleukin; IV, intravenous; PO, per os or by mouth; Q2W, every two weeks; Q4W, every four weeks; SC, subcutaneous

TAM projected at $2.2B By 2030

Significant opportunity and clinical need in hidradenitis suppurativa

- US estimates of **300,000 to 400,000 HS patients**
- **High market need**, 60% of HS patients are biologic eligible
- Tibulizumab may offer **convenient Q4W SC dosing regimen**

Assumes COSENTYX® becomes first line biologic for HS following FDA approval for HS on 31-Oct-2023.
Sources: Medical Literature, MEDACorp KOLs, Company websites, IQVIA, US Department of Veteran's Affairs, Zura Bio Management
Acronyms: HS, hidradenitis suppurativa; Q4W, every four weeks; SC, subcutaneous

We are developing tibulizumab as a differentiated treatment for HS patients

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We are developing tibulizumab to potentially address three critical gaps

01 EFFICACY

Combined IL-17 + BAFF inhibition potentially results in broader and improved clinical responses for HS patients

02 TOLERABILITY

The two components of tibulizumab have been safely administered to ~150,000 study participants or patients[1]

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tibulizumab

ZB-106

Anti-BAFF x IL-17

Tibulizumab, is a humanized bispecific dual antagonist antibody, and has been engineered to bind to and neutralize both BAFF and IL-17A. Our approach with tibulizumab is to inhibit both pathways with a single agent, potentially providing clinical benefits to a broader range of patients, as well as a greater level of effect.

systemic sclerosis (SSc)

Initial area of development in orphan disease, systemic sclerosis

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Systemic sclerosis is a rare & life-threatening disease with no approved therapy

~200,000
people with SSc in US, EU and Japan [1]

40-60%
mortality in 10 years [2]

Zero
SSc-specific * drugs approved

$2B+
annual potential market opportunity

Sources: Medscape, BMJ best practice [1] Health Advanced, LLC; Lenabasum Commercial Market Assessment. [2] Tyndall et al, 2010 [3] Bergamasco, A. et al., Clin Epidemiol. 2019 Apr 18;11:257-273 [4] Zura Bio internal analysis and benchmarking, [5] Internal assumption based on demand research and rare disease analogues

(*) no effective treatment exists that combats the disease across organ systems

No effective treatment exists that combats the disease across organ systems

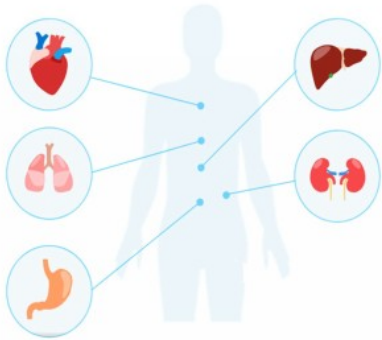
Systemic sclerosis is characterized by tissue inflammation and fibrosis

Lung

*Two disease-modifying drugs are approved for severe lung complications of the disease (SSc-ILD)

Skin

Other Organs



Tibulizumab has the potential to provide broader efficacy, working in more patients not just certain subsets

IL-17 and BAFF-Mediated Inflammation both contribute to SSc progression

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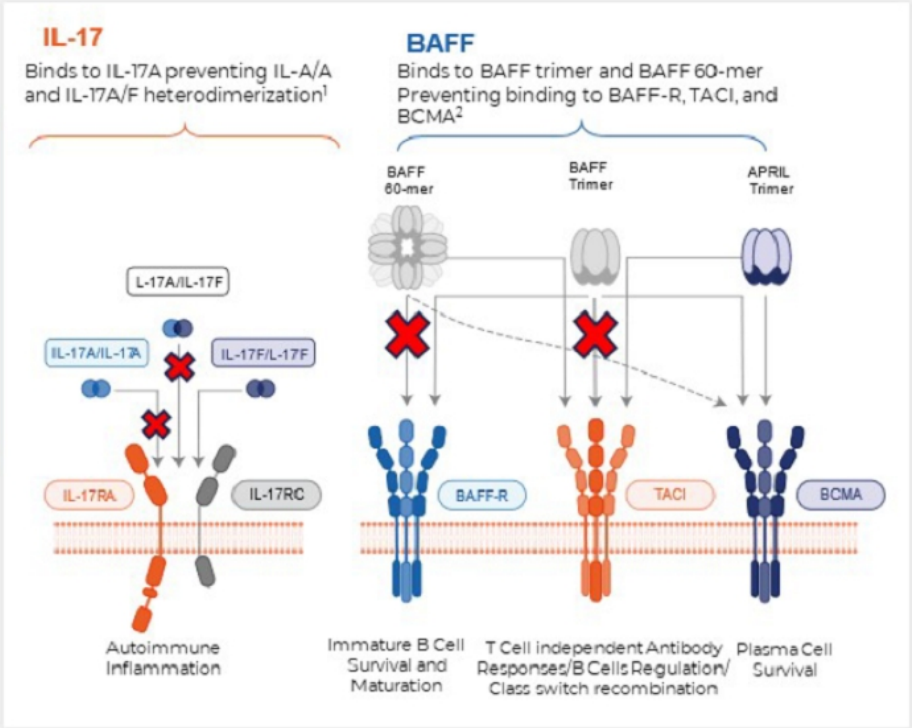
SSc includes the presence of autoantibodies, and aberrant activation of B-cells, T-cells, and cytokines

IL-17 is a pro-inflammatory cytokine that has been identified as a key contributor to SSc progression.

- IL-17 is increased in skin lesions and peripheral blood[1,2]
- Neutralization of IL-17 protected against bleomycin induced fibrosis[3]



B cell activating factor (BAFF) is a potent B-cell activator and promotes the survival and differentiation of B-cells.

- BAFF is increased in peripheral blood and correlates with skin fibrosis and incidence of pulmonary fibrosis[4,5]
- In pre-clinical models BAFF blockade prevents skin fibrosis & autoantibody production[6,7]

Combined approaches to address T-cell and B-cell drivers of autoimmunity have the potential to increase clinical benefit

Sources: [1] Zhou et al. Human Immunology 2015; [2] Yang et al. Arthritis Res Ther 2014; [3] Cipolla et al. FASEB 2017; [4] Matsushita et al. Arthritis Rheum 2006; [5] Matsushita et al. J Rheum 2007; [6] Matsushita et al. J Invest Dermatol 2007; [7] François et al. J Autoimmun 2015

Synergistic benefit of IL-17 and BAFF Neutralization has been demonstrated in classic Collagen Induced Arthritis (CIA) model

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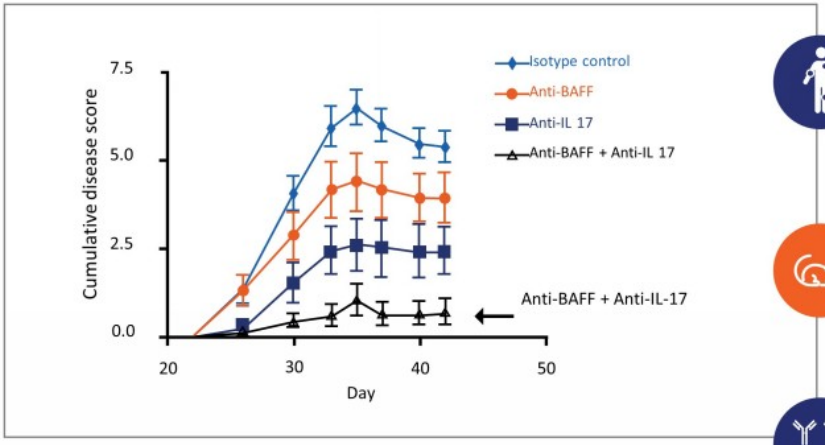

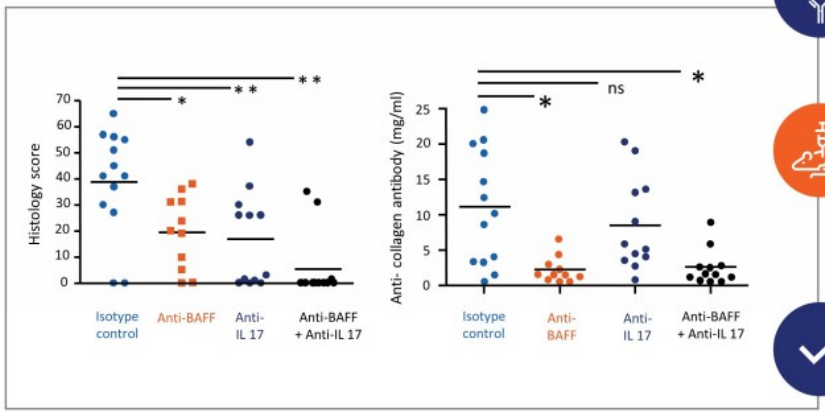

Rheumatoid arthritis is a prototypic autoimmune disease where individually targeting **IL-17-mediated inflammation or depleting B cells** has been clinically validated

The CIA murine model is similarly characterized by **increased IL-17 production** and B cells that drive disease pathogenesis

Surrogate antibodies were used to evaluate whether **neutralization of IL-17 and BAFF** was superior to targeting individual pathways

Mice were injected with **anti-IL-17A and/or anti-BAFF** on days 22, 29, and 36

Blockade of both IL-17A and BAFF was associated with reduced:

- **Disease severity**
- **Anti-collagen antibodies**
- **Inflammation in the hind paw (histology score)**

Sources: Zura Internal Data, IND Briefing

Tibulizumab is Clinically De-Risked Through Phase 1b

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78 Participants Dosed Across Three Phase 1/1b studies

57 participants with single dose; 21 participants with multiple dose up to 12 weeks

PHARMACOKINETICS

- $t_{1/2}$ is 26.9 days
- Bioavailability after SC doses was 62.9%
- At doses tested there is evidence of maximum target engagement with clinical safety supporting 6-fold "window" between max target engagement and max human dose tested

Established dosing regimen

PHARMACODYNAMICS

- In Phase 1b studies in both RA and Sjögren's there were multiple impacts on PD markers:
  - Decrease in CD20+ B-cells with higher doses generally associated with larger changes from baseline
  - Decrease in hs-CRP AUC was associated with higher ZB-106 AUCs

Demonstrated PD in participants in Ph1b

SAFETY and ADA

- SAD Studies: No deaths or SAEs
- MAD study: No deaths, single related SAE of neutropenia with resolution
- Most frequent TEAE: Headache, transient neutropenia, nausea, diarrhea
- No TEAE of infection at target doses
- In the MAD study, one participant had TE-ADAs detected at a low titer

Safety / ADA profile in line with TALTZ®

Tibulizumab is a highly validated molecule that enables the opportunity to deliver on the promise of both IL-17 and BAFF inhibition in autoimmune disease

Abbreviations: MAD, multiple ascending dose; SAD, single ascending dose

Phase 2 SSc study focused on skin/lung endpoints

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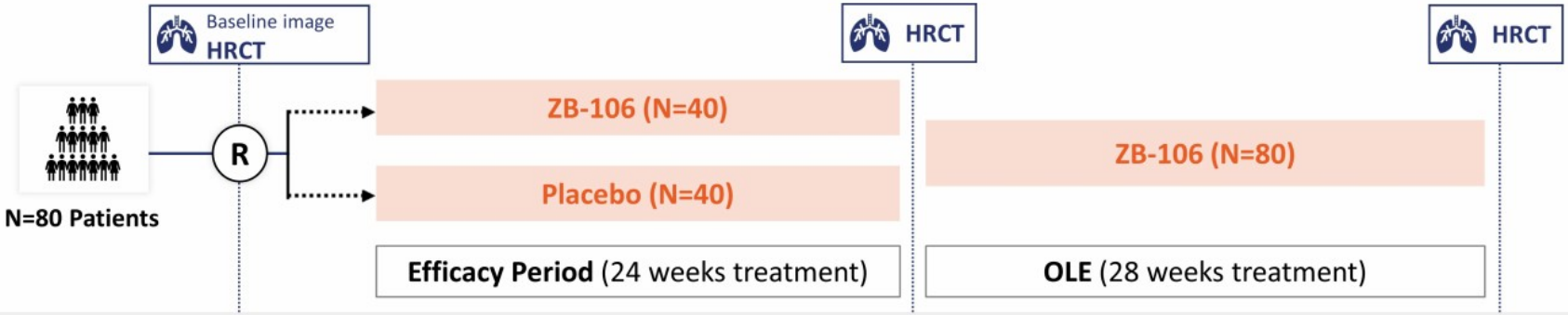
Key Inclusion Criteria

- Early diffuse cutaneous SSc, enriched for SSc-ILD
- mRSS 15-45
- Disease duration < 5years
- Stable background therapy, including MMF for 6 months
- Anti-centromere antibody negative

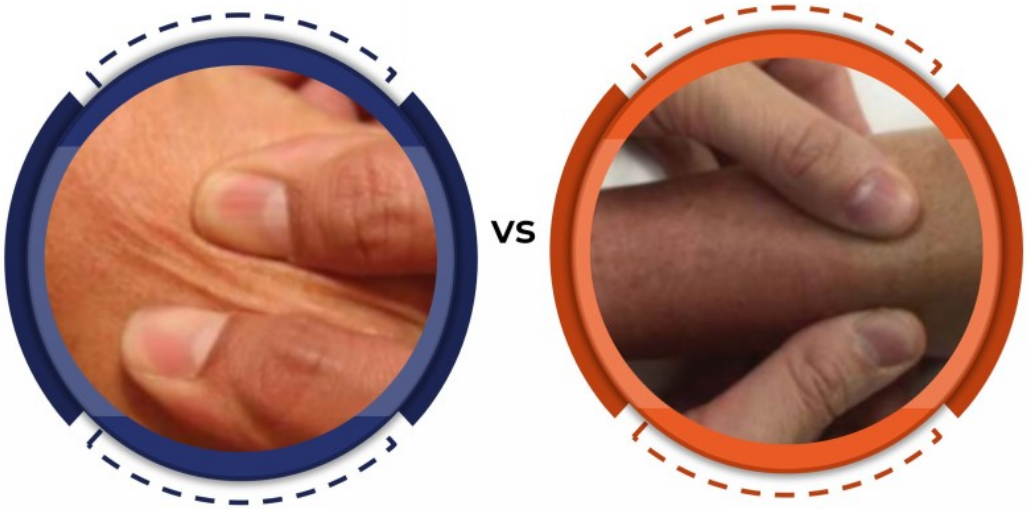
Randomized Trial (mRSS and HRCT)



Key Efficacy Endpoints

mRSS (Primary)	qHRCT / FVC	HAQ-DI (Function)	Clinician / Patient Global

Assessing Skin Thickness and Fibrosis with modified Rodnan skin score (mRSS)

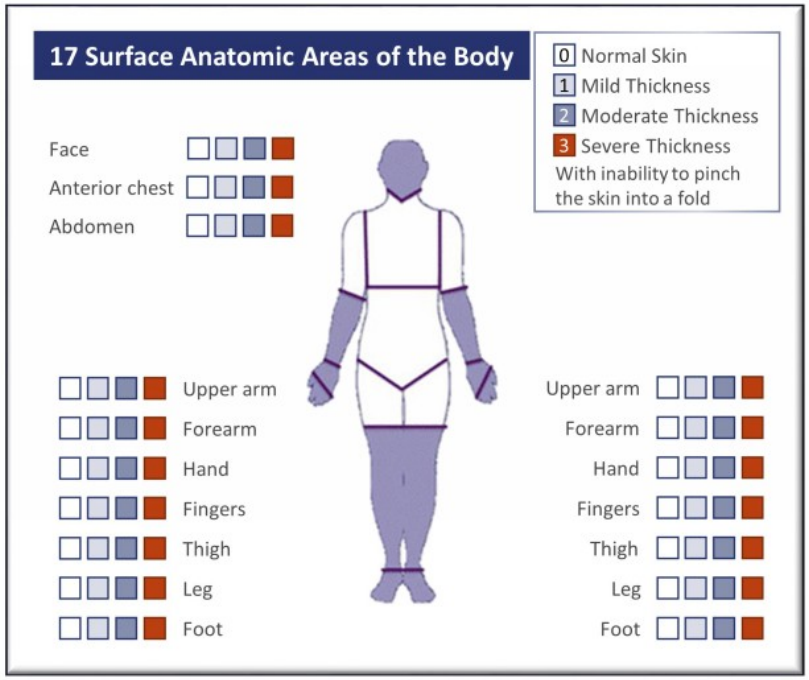


Fine Wrinkles (0/3) VS **Severe Thickness (3/3)**

Severe skin thickening and tightening restricts movement and causes painful ulcers on the hands and fingers, significantly impairing daily activities and quality of life.

The **mRSS assesses skin thickness** in systemic sclerosis patients by **evaluating 17 body sites** (e.g., face, chest, abdomen, arms, legs). Each site is scored from 0 to 3.

The total score ranges from 0 to 51, with **higher scores indicating greater skin involvement**.



Assessing Interstitial Lung Disease (ILD) progression in SSc

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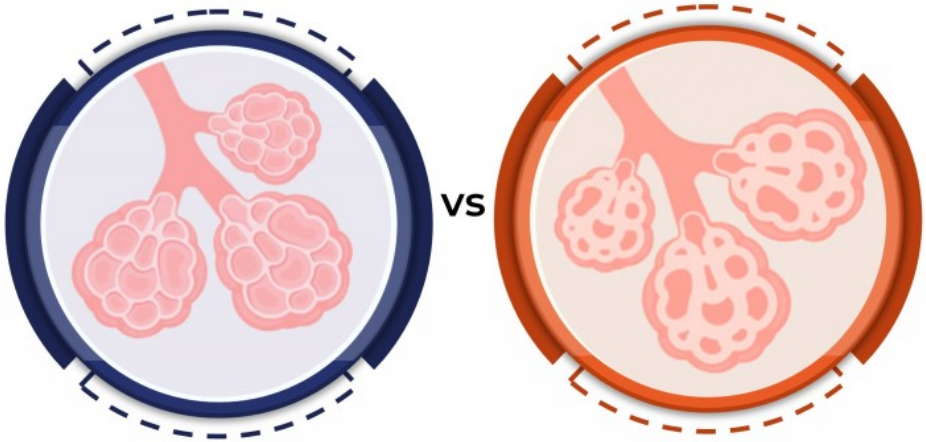
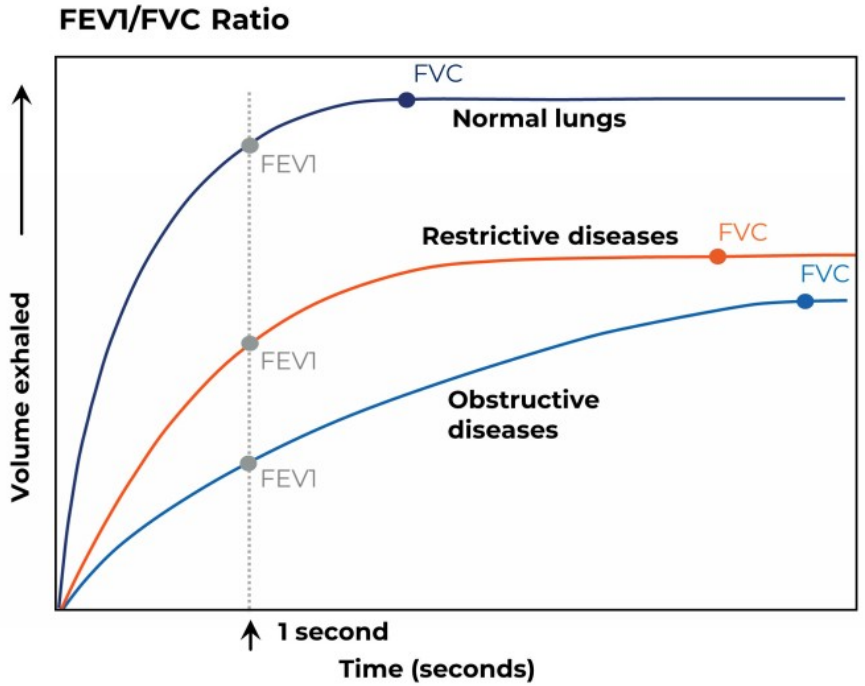


ILD encompasses a diverse group of pulmonary disorders characterized by inflammation and progressive fibrosis of the lung interstitium, leading to restrictive lung physiology and impaired gas exchange.

SSc often leads to ILD due to immune system dysregulation and subsequent lung interstitium fibrosis.



Phase 2 SSc development aims to reduce historical risks associated with therapeutic area development

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Historic drivers of SSc study failures

1. Novel, and unvalidated mechanisms
2. Inclusion/exclusion criteria misses
3. Balancing sample size for mRSS and ILD participants

Increase probability of success

1. Larger study sample size increases probability of success (mRSS)
2. Sufficient sample size for ILD to understand potential Phase 3 effect
3. High Resolution CT highly correlates with FVC > ILD read-through

Acronyms: CT, computed tomography; FVC, forced vital capacity; IL, interleukin; ILD, interstitial lung disease; mRSS, modified Rodnan skin score

tibulizumab

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Anti-BAFF x IL-17

Tibulizumab, is a humanized bispecific dual antagonist antibody, and has been engineered to bind to and neutralize both BAFF and IL-17A. Our approach with tibulizumab is to inhibit both pathways with a single agent, potentially providing clinical benefits to a broader range of patients, as well as a greater level of effect.

hidradenitis suppurativa (HS)

TAM projected at $3.5 -$4B By 2030

Overview of hidradenitis suppurativa (HS)

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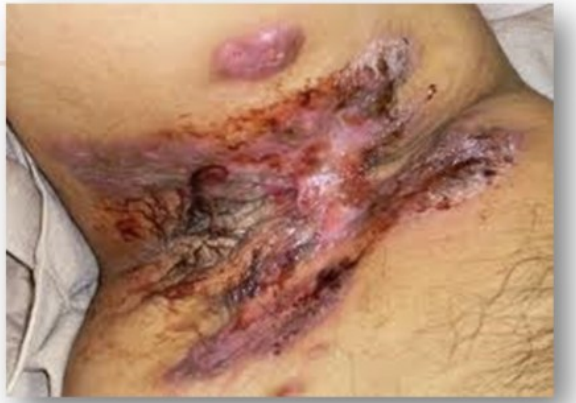
DISEASE OVERVIEW

- Hidradenitis suppurativa is an inflammatory follicular skin disease
- Skin lesions develop in axillae, in the groin, and under the breasts, are formed as a result of inflammation & infection of sweat glands and are characterized by:
  - Recurrent boil-like nodules and abscesses that culminate in pus-like discharge
  - Difficult-to-heal open wounds (sinuses) and scarring
  - Increased Th1/Th17 and B cell mediated inflammation [1-3]
  - Disproportionately affects women between adolescent age to 55 years of age [4,5]



CLINICAL OPPORTUNITY [6]

Estimated

~300K people

living with Hidradenitis suppurativa in the U.S.

(1-2% global prevalence)

Average of

7 years

to diagnose globally

High unmet need

>50% patients still left inadequately treated

According to HiSCR 75 data

CURRENT APPROVED TREATMENTS ONLY AIM TO MANAGE SYMPTOMS AND INCLUDE STEROIDS OR IMMUNOSUPPRESSANTS TO MANAGE SYSTEMIC SYMPTOMS

Sources: [1] Moran, Barry, et al. Journal of Investigative Dermatology, doi:10.1016/j.jid.2017.05.033. [2] Banerjee, Anirban, et al. Immunological Investigations, doi:10.1080/08820139.2016.1230867. [3] Sabat, Robert, et al. Journal of Allergy and Clinical Immunology, doi:10.1016/j.jaci.2022.10.034. [4] Garg, Amit, et al. JAMA Dermatology, doi:10.1001/jamadermatol.2017.0201. [5] Ingram, John R. British Journal of Dermatology, doi:10.1111/bjd.19435. [5] Ingram, John R. British Journal of Dermatology, doi:10.1111/bjd.19435. [6] Medical Literature, MEDACorp KOL Discussions

B Cell Signaling Potentiates HS Disease

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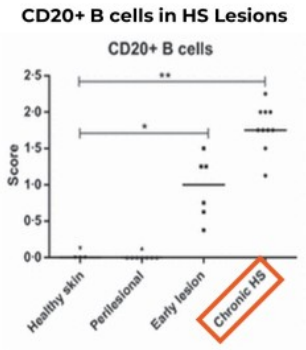
Pathogenic Role for B Cells and Plasma Cells

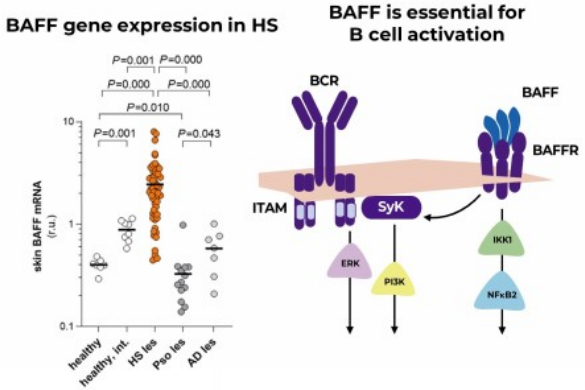
- CD20+ B and CD138+ Plasma Cells are increased in chronic HS lesions [1]



- B cell depletion with rituximab provided therapeutic benefit with 4 out of 5 cases reporting complete remission of HS lesions [5]

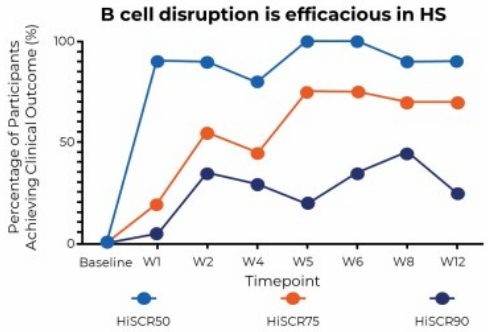
BAFF Drives B Cell Activation and Inflammation

- Increased BAFF expression in HS lesions and tunnels [2-4]
- Neutralization of BAFF in HS lesional explants reduced the expression of B & plasma cell gene signatures [2]



Clinical Benefit of Targeting B Cells

- Modulating B cell function using fostamatinib (SYK inhibition) provided therapeutic benefit in HS [6]
- B cell depletion with rituximab provided therapeutic benefit [5]
- 4/5 cases report complete remission of HS lesions [5]



Week 12	% Achieving HiSCR50	% Achieving HiSCR75
Fostamatinib (SYK inhibition)[6]	85%	70%

Sources: [1]Van der Zee, H.H., et al. British Journal of Dermatology, doi:10.1111/j.1365-2133.2011.10698.x. [2]Rumberger, Beth E., et al. Inflammation Research, doi:10.1007/s00011-020-01381-7. [3]Sabat, Robert, et al. Journal of Allergy and Clinical Immunology, doi:10.1016/j.jaci.2022.10.034. [4]Gudjonsson, Johann E., et al. JCI Insight, doi:10.1172/jci.insight.139930. [6]Jepsen, Rebecca, et al. Journal of the American Academy of Dermatology, doi:10.1016/j.jaad.2023.05.076.

Ongoing Novartis phase 2b multicenter platform study offers additional clinical evidence of B cell targeting benefit in HS

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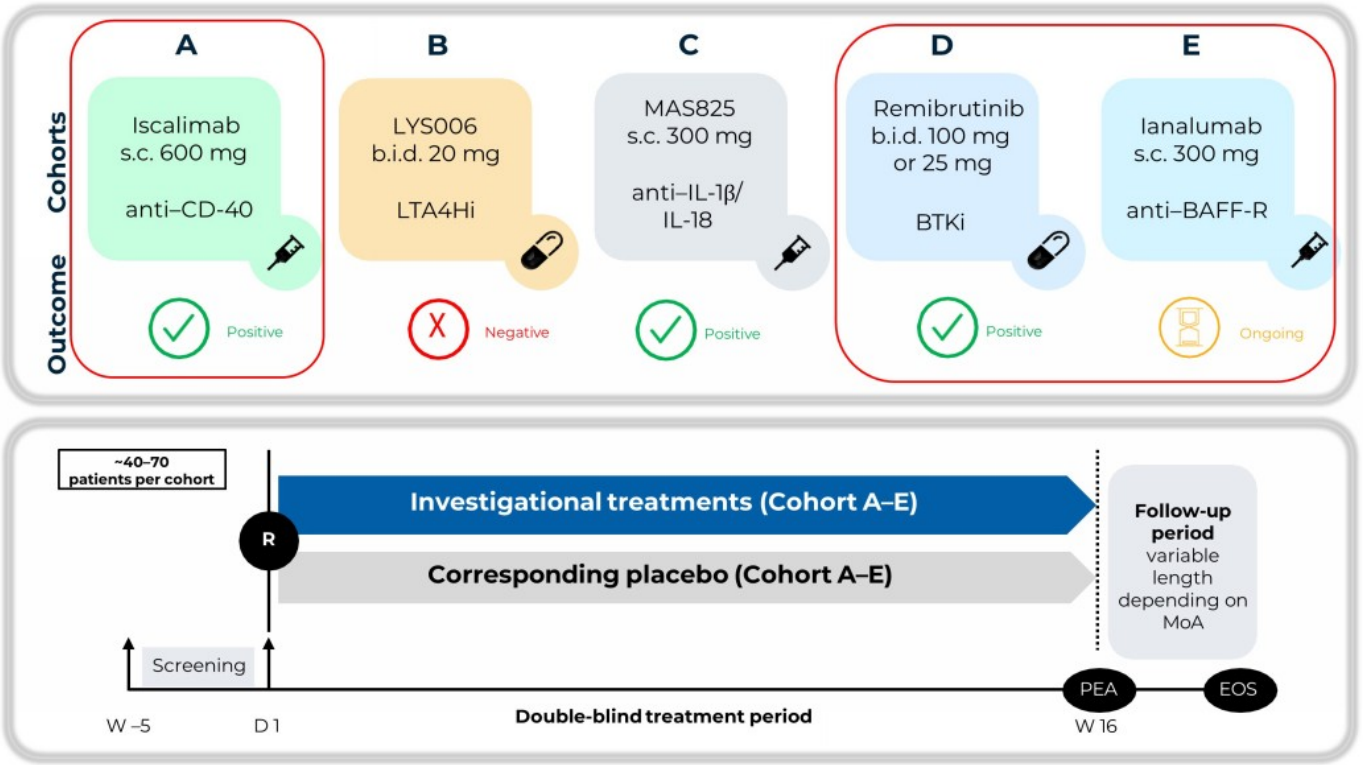
Presented at the American Academy of Dermatology Annual Meeting; March 8–12, 2024; San Diego, CA.



Patients

- Adult patients aged 18–65 years
- Moderate to severe HS for ≥12 months in ≥2 anatomical areas with ≤15 tunnels
- ***Cohorts A, C, and E:*** ≥5 inflammatory lesions
- ***Cohorts B and D:*** ≥3 inflammatory lesions

*Study started in February 2019 and is currently ongoing.
BAFF-R, B-cell activating factor of the tumor necrosis alpha family receptor; b.i.d., twice daily; BTKi, Bruton's tyrosine kinase inhibitor; CD, cluster of differentiation; D, day; EOS, end of study; HS, hidradenitis suppurativa; IL, interleukin; LTA4H, leukotriene A4 hydrolase; MoA, mechanism of action; PEA, primary endpoint analysis; R, randomization; s.c., subcutaneous; W, week. Clinicaltrials.gov NCT03827798. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03827798 (Accessed 6 Mar 2024).

Novartis' interim results presented at '24 AAD, BTKi PBO adjusted delta in line with approved and in development agents

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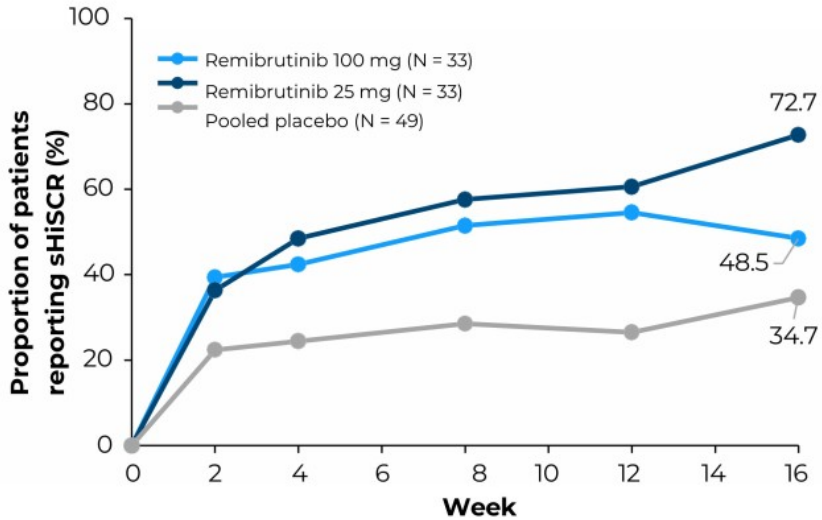
Presented at the American Academy of Dermatology Annual Meeting; March 8–12, 2024; San Diego, CA.

- The primary endpoint of this study was met for both doses of remibrutinib; patients treated with remibrutinib reported a greater rate of sHiSCR* at Week 16 compared with placebo

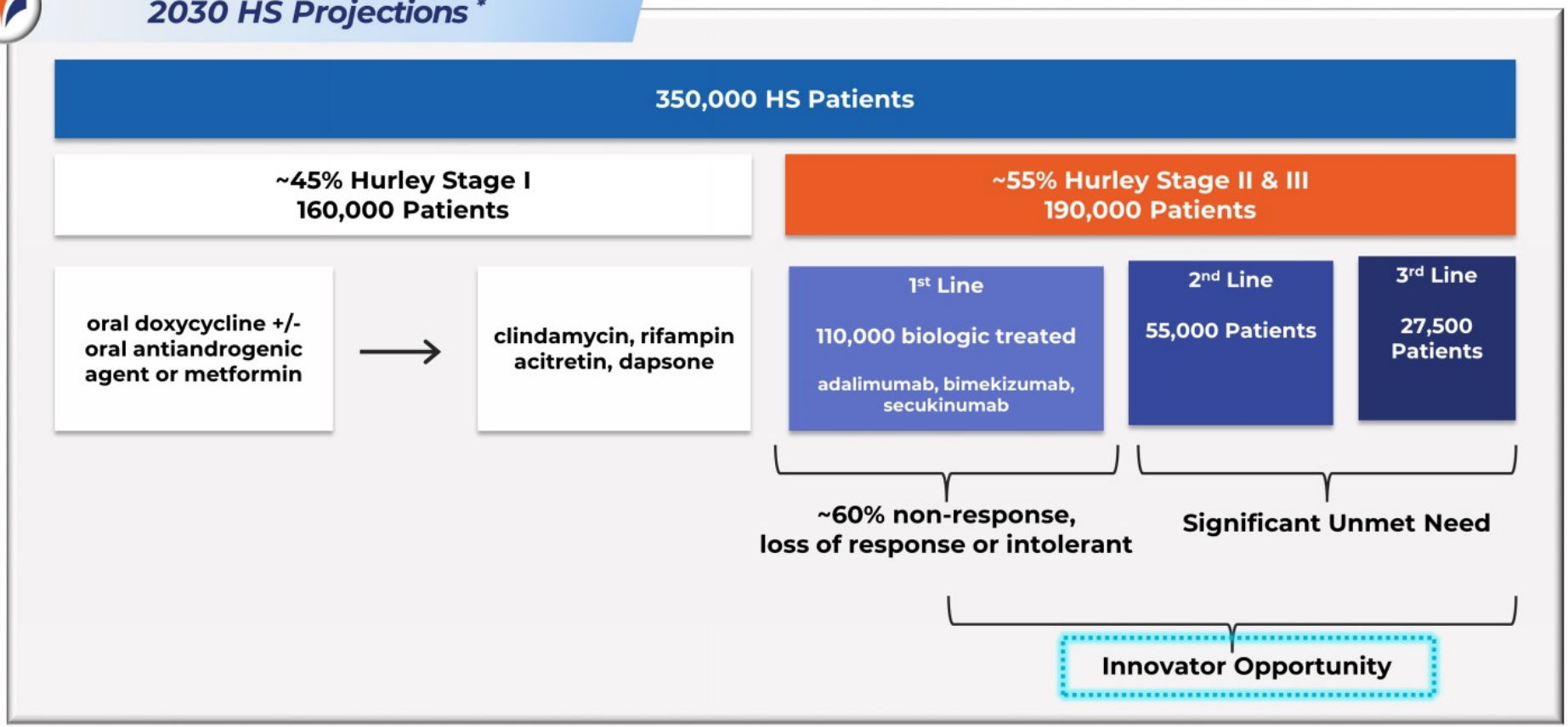
	Cohort D		Cohort A–D
	Remibrutinib 25 mg (N = 33)	Remibrutinib 100 mg (N = 33)	Pooled Placebo (N = 49)
Proportion of patients with sHiSCR*:			
Observed with NRI (%)	**72.7**	**48.5**	**34.7**
Difference† (%) (95% CI)	38.0 (21.1 to 55.0)	13.8 (–4.4 to 32.0)	
Bayesian estimated (%)	**72.3**	**48.5**	**34.9**
Difference† (%) (95% CI)	37.2 (19.7 to 53.0)	13.9 (–4.2 to 31.9)	
Probability of difference‡	99.9	89.6	



*The sHiSCR is defined as a ≥50% reduction in the abscess and inflammatory nodule count and no increase in draining tunnels compared with baseline. †Difference refers to the difference between remibrutinib (either dose) and pooled placebo at Week 16. ‡Bayesian posterior probability of remibrutinib (either dose) being better than pooled placebo.
CI, confidence interval; HiSCR, hidradenitis suppurativa clinical response; n, total number of patients with response; N, total number of patients in each treatment arm; NRI, non-responder imputation; sHiSCR, simplified hidradenitis suppurativa clinical response.

HS innovator expected to be uniquely positioned to capture opportunities across 1st, 2nd, and 3rd-line HS patients

2030 HS Projections *



(*) Assumes Cosentyx® becomes first line biologic for HS following FDA approval for HS on 31-Oct-2023.
Sources: Medical Literature, MEDACorp KOLs, Company websites, IQVIA, US Department of Veteran's Affairs, Zura Bio Management
Acronyms: HS, hidradenitis suppurativa

Planned Phase 2 HS Trial Design*

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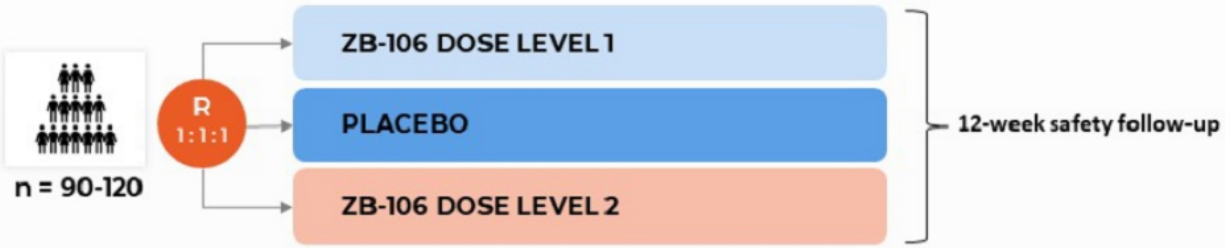
KEY INCLUSION CRITERIA

- Moderate to Severe HS
- Hurley Stage II/III
- Total abscess and inflammatory count (AN) ≥ 5



KEY EFFICACY ENDPOINTS

- HiSCR
- Improvement in baseline AN counts
- IHS4
- PGA
- DLQI
- PK / PD assessments

KEY SAFETY ENDPOINTS

- General Safety and Tolerability
- Severe infection
- Neutropenia

(*) Trial design is subject to change

Acronyms: DLQI, dermatology life quality index; HiSCR, Hidradenitis Suppurativa Clinical Response; HS, hidradenitis suppurativa; IHS4, international hidradenitis suppurativa severity score system; PD, pharmacodynamic; PGA, physician's global assessment; PK, pharmacokinetic; R, randomization

crebankitug

ZB-168

Anti-IL-7Rα + TSLP

Crebankitug is a high-affinity, fully human monoclonal antibody that neutralizes the IL-7 receptor alpha (IL-7Rα) chain, potentially blocking the immune pathways of IL-7 and thymic stromal lymphopoietin (TSLP).

Crebankitug, a multi-functional antibody with cytokine signaling via IL-7R and TSLP pathways

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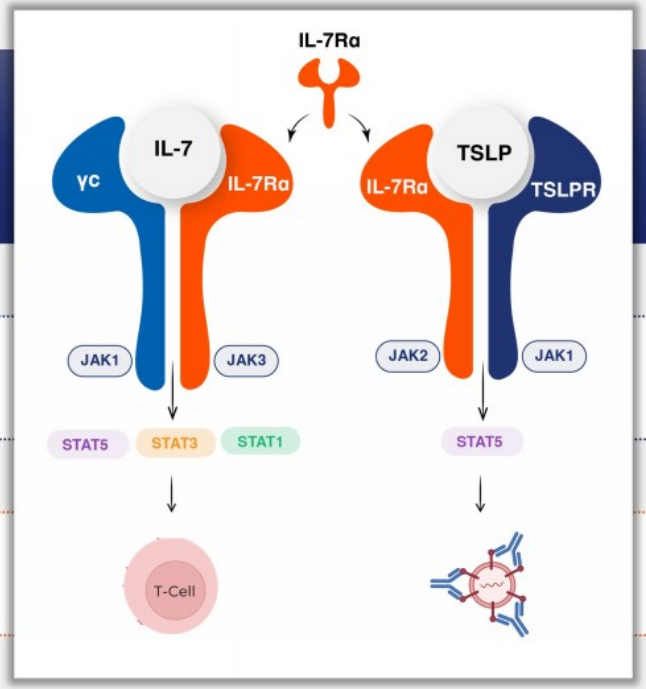
IL-7Rα is a key receptor in immune regulation, central to the signaling of cytokines ***IL-7*** and ***TSLP***

IL-7

IL-7Rα collaborates with the common gamma chain (γc) to establish the IL-7 receptor complex

Triggers a sequence of cellular events, notably **JAKs & STATs**

Vital for the growth, sustenance, and balance of T-cells



TSLP

TSLP binds to its dedicated receptor, TSLPR. For optimal signaling, IL-7Rα joins the mix, creating a composite complex with TSLPR and TSLP

This assembled complex **initiates pathways** primarily linked to **type 2 immunity**

Commonly tied to allergic responses and specific inflammatory scenarios

Positioning crebankitug for diverse immune-related and autoimmune conditions

Both TSLP and IL-7 have a role in activating Th1, Th2 and Th7 driven inflammation

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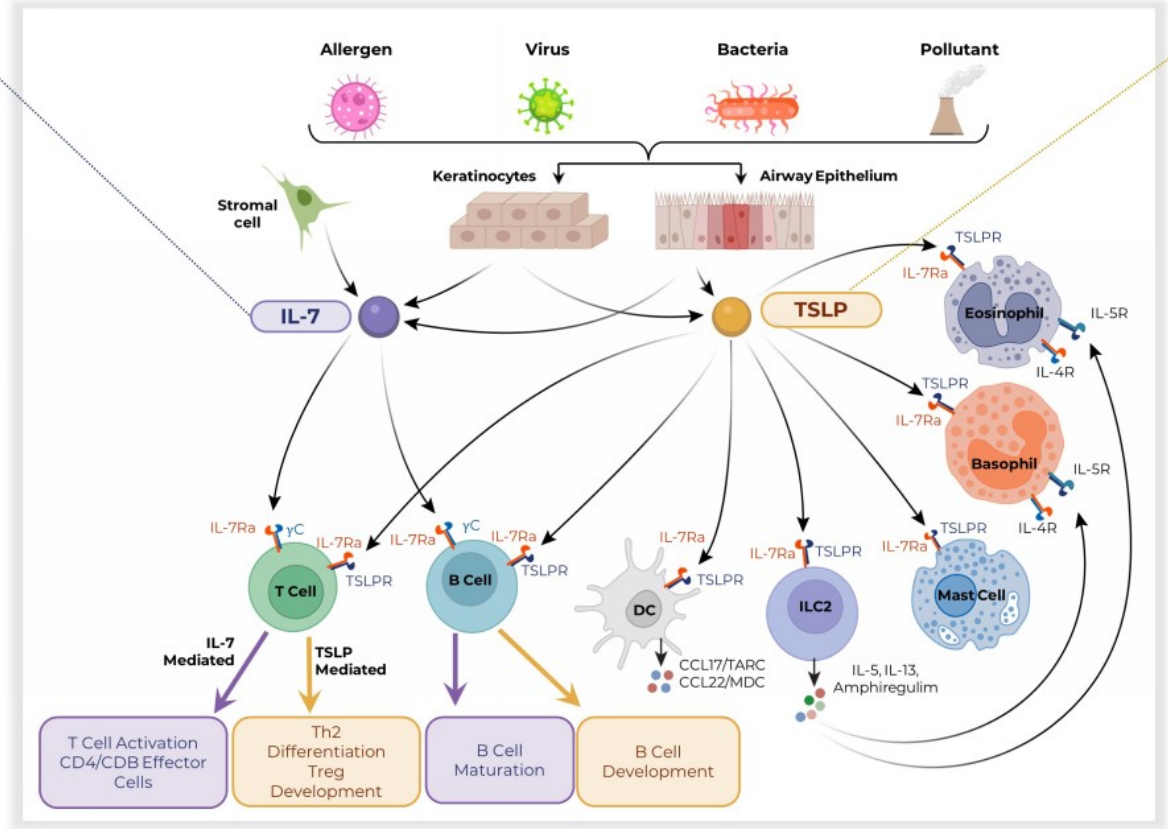
IL-7 PATHWAY

- IL-7 is a growth factor that binds to the heterodimeric receptor of IL-7R:γC and is critical for the survival, development and homeostasis of central and effector memory T cells[4]
- Due to the high expression of IL-7R on T_{eff} compared to T_{reg}, inhibition results in a 20-fold greater activity in reducing T_{eff}, leading to an increase in T_{reg}:T_{eff} ratio[5, 6]



TSLP PATHWAY

- Thymic stromal lymphopoietin (TSLP) is an epithelial-derived cytokine primarily expressed in the lungs, skin and gastrointestinal tract[1]
- TSLP is released from the epithelium by disease amplifying Th2 immune response, including the production of IL-4, -5, -9 and -13.[1]
- TSLP inhibition is clinically validated in severe asthma and has shown positive therapeutic benefit in additional Th2 driven diseases[2,3]

Sources: 1. Ebina-Shibuy, 2022. Nat Rev Immunol, 2. Marone, 2019. Expert Opin Investig Drugs, 3. Menzies-Gow, 2020. Respir Res, 4. Chen, 2021. Frontiers Immunol, 5. Herold, 2019 JCI Insight, Graphic created in BioRender; 5. doi.org/10.3389/fimmu.2018.02692, 6. doi.org/10.1016/j.isci.2020.101421, 7. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01557/full

torudokimab

ZB-880

Anti-IL-33

Torudokimab is a fully human, high affinity monoclonal antibody that neutralizes IL-33, preventing ST2-dependent and ST2-independent (e.g., RAGE) inflammation.

Torudokimab Asset Overview

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About torudokimab

01 IL-33 implicated in driving Th2 biology through ST2 and Th1/Th17 through alternative signaling[1]

02 Well tolerated in Ph1 and Ph2 trials conducted by Eli Lilly[2]

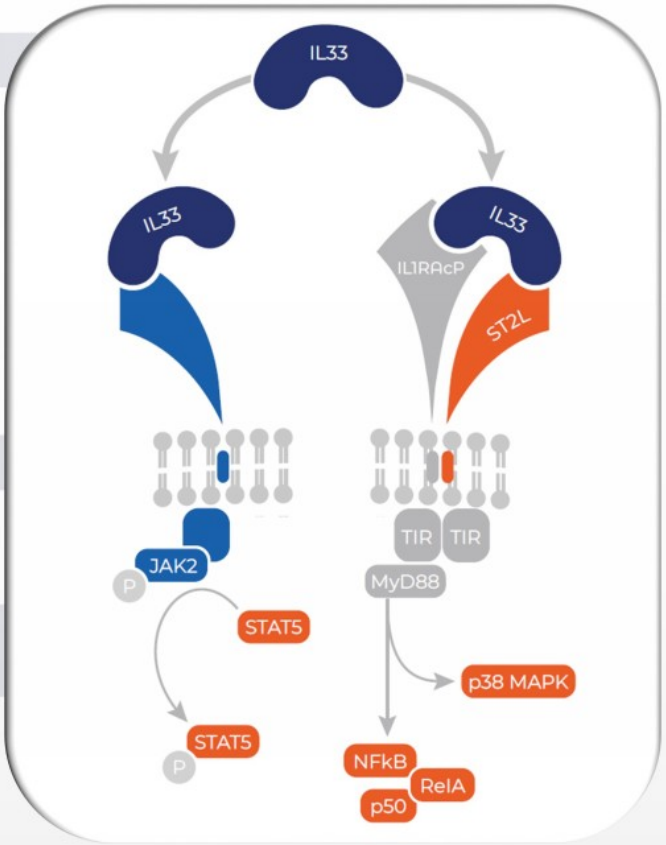
- 141 healthy volunteers in Ph1 study
- 103 participants with moderate to severe atopic dermatitis in Ph2

03 The target engagement evaluation suggested binding to IL-33 and treatment emergent ADA had no apparent impact on PK or target engagement

- Analyses confirmed key biomarker reductions (IL-13, periostin and CCL17/TARC) and no ADA impact[3]
- Potential utility in diseases driven by epithelial inflammation[1]

Mechanism of Action

01 Inhibition of IL-33 blocks both ST2 and RAGE signaling[4]



Initial Focus on Respiratory, Dermatologic, Gastrointestinal and Orphan Autoimmune Indications

01 Potential for 1st-in-class opportunities

02 Validated pathways in COPD4 and asthma[5]

Sources: 1. Cohen et al. 2015 Nature, 2. https://clinicaltrials.gov/ct2/show/NCT03913260; https://clinicaltrials.gov/ct2/show/NCT03343587; https://clinicaltrials.gov/ct2/show/NCT03831191, Section 6.1, DSUR for period 23-Sep-2019 to 22-Sep-2020, 3. doi.org/10.1111/bjd.21631 4. Okragly et al Journal of Inflammation Research 2021:14 3823–3835, 5.. doi:10.1056/NEJMoa2024257

Torudokimab IL-33 Pathway

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IL-33 is a member of the IL-1 cytokine family that is constitutively expressed in structural and lining cells including fibroblasts, endothelial, and epithelial cells of skin, gastrointestinal tract, and lungs[1]

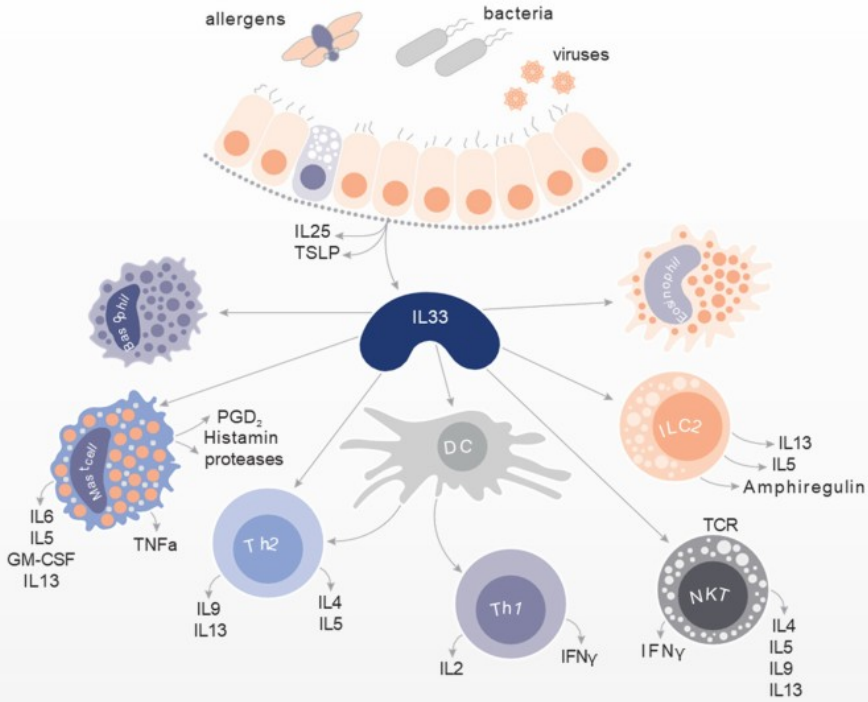
IL-33 is released from the epithelium by disease exacerbating environmental factors and is an important amplifier of innate inflammation during exacerbations[2]

Polymorphisms in IL-33 and ST2 are associated with increased eosinophil production as well as respiratory diseases such as COPD and severe asthma

IL-33 inhibition clinically validated in severe asthma, COPD3, and subsets of other epithelial disorders[4]

Pre-clinical data demonstrates superior activity of torudokimab compared with etokimab suggesting the potential for best-in-class activity[5]

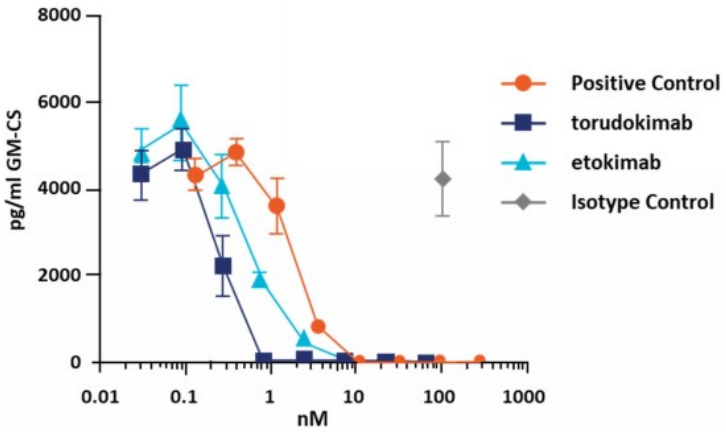
Emerging biology suggests expanding opportunity for IL-33 in fibrotic and autoimmune conditions[6]

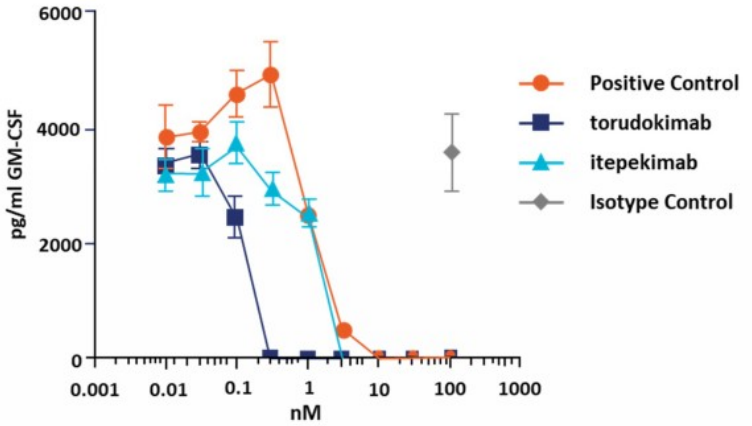


Sources: 1. Chan, 2019. Frontiers Immunol, 2. doi.org/10.1016/j.cyto.2022.155891, 3. https://doi.org/10.1038/ng.323 and doi:10.1016/j.jaci.2020.04.051 , 4. .:https://doi.org/10.1016/S2213-2600(22)00005-4; doi:10.1056/NEJMoa2024257 and doi: 10.1126/scitranslmed.aax2945 , 5. Sci Trans Med., Zura Bio Internal data, 6. doi: 10.1111/imm.12174; https://doi.org/10.3389/fphys.2021.781012 and https://doi.org/10.3389/fmed.2021.739489

Torudokimab Has Potential for "Best-in-Class" Activity

Torudokimab was 2.9 and 5.5-fold more potent than etokimab and itepekimab, respectively, inhibiting IL-33-induced GM-CSF production by human mast cells





Antibody	k_{on} ($M^{-1}s^{-1}$)	k_{off} (s^{-1})	k_d (pM)	Torudokimab Potency
torudokimab (LY3375880)	1.7×10^{6}	6.7×10^{-5}	39	
etokimab (AnaptysBio)	9.4×10^{5}	1.2×10^{-4}	112	**2.9x**
itepekimab (Regeneron)	7.6×10^{5}	1.6×10^{-4}	215	**5.5x**

Sources: Zura Bio Internal data

