**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**PURSUANT TO SECTION 13 OR 15(D)**
**OF THE SECURITIES EXCHANGE ACT OF 1934**

**Date of Report (Date of earliest event reported): April 27, 2023**

## Zura Bio Limited

**(Exact name of registrant as specified in its charter)**

| Cayman Islands | 001-40598 | 98-1725736 |
|---|---|---|
| (State or other jurisdiction of incorporation) | (Commission File Number) | (I.R.S. Employer Identification No.) |

**4225 Executive Square, Suite 600**
**La Jolla, CA 92037**
**(Address of principal executive offices, including zip code)**

**(858) 247-0520**
**(Registrant's telephone number, including area code)**

**(Former name or former address, if changed since last report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communication pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Class A Ordinary Shares, par value $0.0001 per share | ZURA | The Nasdaq Stock Market |
| Warrants, each whole warrant exercisable for one Class A Ordinary Share at an exercise price of $11.50 per share | ZURAW | The Nasdaq Stock Market |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 7.01 Regulation FD Disclosure**.

On April 27, 2023, Zura Bio Limited, a Cayman Islands exempted company (the "Company") issued the press release attached hereto as Exhibit 99.1 to this Current Report on Form 8-K.

Furnished as Exhibit 99.2 hereto and incorporated into this Item 7.01 by reference is an investor presentation (the "Investor Presentation") that the Company has prepared for use in presentations to potential PIPE investors.

By filing this Current Report on Form 8-K and furnishing the information contained herein, the Company makes no admission as to the materiality of any information in this report that is required to be disclosed solely by reason of Regulation FD.

The information contained in the Investor Presentation is summary information that is intended to be considered in the context of the Company's Securities and Exchange Commission ("SEC") filings and other public announcements that the Company may make, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report, although it may do so from time to time as its management believes is warranted. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases or through other public disclosure.

The information presented in Item 7.01 of this Current Report on Form 8-K and Exhibits 99.1 and 99.2 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, unless the Company specifically states that the information is to be considered "filed" under the Exchange Act or specifically incorporates it by reference into a filing under the Securities Act of 1933, as amended, or the Exchange Act.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

| Number | Description |
|---|---|
| 99.1 | Press Release, dated April 27, 2023. |
| 99.2 | Investor Presentation |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document). |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: April 27, 2023

**Zura Bio Limited**

By: /s/ Someit Sidhu
Someit Sidhu
Chief Executive Officer

**Exhibit 99.1**

# Zura Bio Announces $80 Million Financing and the Licensing of Tibulizumab (ZB-106), a Potential First-in-Class anti-IL-17 and anti-BAFF Dual Antagonist for Autoimmune Diseases

- *Licensing a potential first-in-class, anti-IL-17 and anti-BAFF dual antagonist*
- *In connection with the transaction, Zura Bio announces pricing of $80 million private placement financing*

SAN DIEGO, California -- April 27, 2023 — Zura Bio Limited (Nasdaq: "ZURA") ("Zura" or "Zura Bio"), a multi-asset clinical-stage biotechnology company focused on developing novel medicines for immune and inflammatory disorders, today announced the license from Eli Lilly and Company ("Lilly") of tibulizumab, a potential first-in-class, anti-IL-17 and anti-BAFF dual antagonist. Following the closing, the compound will be known as ZB-106.

ZB-106 currently has clinical data from two Phase 1b studies completed in Rheumatoid Arthritis and Sjogren's Syndrome. The safety profile to date appears to be acceptable, with no new findings relative to known IL-17 and BAFF inhibitors. Chronic toxicology studies have been completed with no adverse drug-related findings.
Zura plans to initiate a Phase 2 study for ZB-106 in Systemic Sclerosis in 2024 to be followed by a study in Hidradenitis Suppurativa.

Dr. Someit Sidhu, Chief Executive Officer and Director of Zura Bio stated, "We believe tibulizumab is a great complement to our existing multi-asset pipeline. This is the second asset Zura Bio has licensed from Lilly in less than one year. We value their continued partnership and global presence as a leader in the inflammatory disease space and are grateful for the work they have done to progress this asset to its current state. We are excited to advance ZB-106 with the potential to evolve research and impact patients across a number of inflammatory diseases."

**Private Placement Financing**

In connection with the closing of the licensing transaction for ZB-106, Zura has agreed to sell an aggregate of approximately 18.8 million Class A ordinary shares, and pre-funded warrants in lieu of Class A ordinary shares, to certain accredited institutional investors in a private placement financing (the "Offering"). The Offering is expected to result in gross proceeds to Zura of approximately $80 million cash, before deducting placement agent fees and other offering expenses payable by Zura. In addition, Lilly has agreed to receive up to an aggregate of approximately $4.25 million in Class A ordinary shares in lieu of a portion of the upfront cash to be paid by Zura as consideration for the licensing transaction for ZB-106.

The Offering was led by Deep Track Capital, Great Point Partners, Suvretta Capital, and a leading life sciences-focused investment fund, alongside several additional new and existing investors.

Pursuant to the terms of the subscription agreement, each Class A ordinary share will be sold at a price of $4.25 per share and each pre-funded warrant will be sold at a price of $4.249 per pre-funded warrant. Each pre-funded warrant will have an exercise price of $0.001 per Class A ordinary share. At the initial closing, investors have committed to purchase an aggregate of approximately 3.8 million Class A ordinary shares for a total of approximately $16 million in gross proceeds, excluding the shares issued to Lilly. At the second closing, expected in the second half of 2023, investors have committed to purchase an aggregate of approximately 15 million Class A ordinary shares and pre-funded warrants for an additional total of approximately $64 million in gross proceeds, subject to shareholder approval for authority to allot such shares and warrants. Upon the final closing of the Offering, Zura anticipates having $120 million in cash and cash equivalents, which it believes will be sufficient to fund its planned operating expenses and capital expenditure requirements through 2026.

Guggenheim Securities served as lead placement agent for the Offering. Raymond James also served as placement agent for the Offering.

The securities are being sold in a private placement and have not been registered under the Securities Act of 1933, as amended, and may not be offered or sold in the U.S. absent registration or an applicable exemption from registration requirements. Zura has agreed to file resale registration statements with the U.S. Securities and Exchange Commission (the "SEC"), for purposes of registering the resale of the Class A ordinary shares and pre-funded warrants issued or issuable in connection with the Offering.

This press release does not constitute an offer to sell or the solicitation of an offer to buy the securities, nor shall there be any sale of the securities in any state in which such offer or sale would be unlawful prior to the registration or qualification under the securities laws of such state. Any offering of the shares under the resale registration statement will only be by means of a prospectus.

**About Zura Bio**

Zura Bio is a clinical-stage biotechnology company advancing immunology assets into Phase 2 development programs, including ZB-168 and torudokimab. ZB-168 is an anti IL7R α inhibitor that has the potential to impact diseases driven by IL7 and TSLP biological pathways. Zura Bio aims to develop a portfolio of therapeutic indications for ZB-168 which builds on existing Phase 1b data in Type 1 Diabetes demonstrating a favorable safety profile and strong biological rationale. Torudokimab is a fully human, high affinity monoclonal antibody that neutralizes IL33 and is currently at the Phase 2 clinical development stage.

**Trademarks**

All product names, brands, and other trademarks mentioned are the property of their respective trademark holders, and use of them does not imply any affiliation with or endorsement by them.

**Forward Looking Statements Disclaimer**

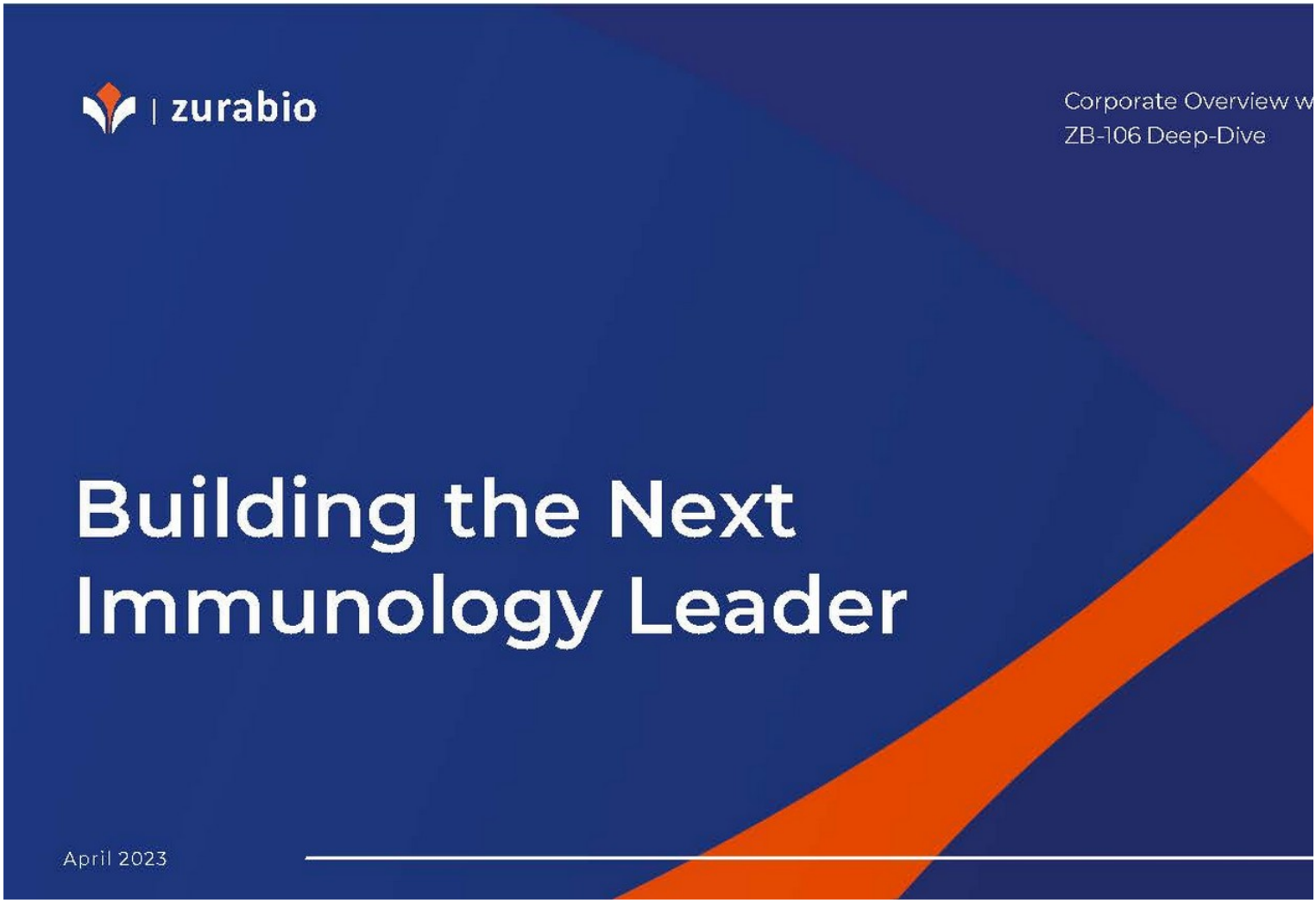
This communication includes "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believe," "predict," "potential," "continue," "strategy," "future," "opportunity," "would," "seem," "seek," "outlook" and similar expressions are intended to identify such forward-looking statements. Forward-looking statements are predictions, projections and other statements about future events that are based on current expectations and assumptions and, as a result, are subject to risks and uncertainties that could cause the actual results to differ materially from the expected results. These statements are based on various assumptions, whether or not identified in this communication. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as, and must not be relied on by an investor as, a guarantee, an assurance, a prediction or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and will differ from assumptions. You should carefully consider the risks and uncertainties described in the "Risk Factors" sections of Zura Bio's filings with the SEC, including, without limitation, the risks and uncertainties described in the Registration Statement on Form S-4, as amended (the "Registration Statement"). These filings would identify and address other important risks and uncertainties that could cause actual events and results to differ materially from those contained in the forward-looking statements. Many of these factors are outside Zura Bio's control and are difficult to predict. Many factors could cause actual future events to differ from the forward-looking statements in this communication, including but not limited to: (1) the outcome of any legal proceedings that may be instituted against Zura Bio following its business combination (the "Business Combination"); (2) volatility in the price of Zura Bio's securities; (3) the inability to realize the anticipated benefits of the Business Combination, which may be affected by, among other things, competition, the ability of Zura Bio to grow and manage growth profitably, maintain relationships with customers and suppliers and retain key employees; (4) costs related to the Business Combination, subsequent financing transactions and the ongoing costs relating to operating as a public company; (5) changes in the applicable laws or regulations; (6) the possibility that Zura Bio may be adversely affected by other economic, business, and/or competitive factors; (7) the risk of downturns and a changing regulatory landscape in the highly competitive industry in which Zura Bio operates; (8) the impact of the global COVID-19 pandemic; (9) the potential inability of Zura Bio to raise additional capital needed to pursue its business objectives or to achieve efficiencies regarding other costs; (10) the enforceability of Zura Bio's intellectual property, including its patents, and the potential infringement on the intellectual property rights of others, cyber security risks or potential breaches of data security; (11) the possibility that Zura Bio's shareholders do not approve the terms of the Offering and failure to satisfy other customary closing conditions in connection with the Offering; and (12) other risks and uncertainties described in the Registration Statement and such other documents filed by Zura Bio from time to time with the SEC. These risks and uncertainties may be amplified by the COVID-19 pandemic, which has caused significant economic uncertainty. Zura Bio cautions that the foregoing list of factors is not exclusive or exhaustive and not to place undue reliance upon any forward-looking statements, including projections, which speak only as of the date made. Zura Bio gives no assurance that it will achieve its expectations. Zura Bio does not undertake or accept any obligation to publicly provide revisions or updates to any forward-looking statements, whether as a result of new information, future developments or otherwise, or should circumstances change, except as otherwise required by securities and other applicable laws.

**Contacts**

**Corporate Contact:**
Kim Davis
Chief Legal Officer
Email: info@zurabio.com
Website: www.zurabio.com

**Media:**
Chris Wilson
Triquartista Consulting
Email: chris@trequartistaconsulting.com

Exhibit 99.2


zurabio
Corporate Overview w
ZB-106 Deep-Dive
Building the Next Immunology Leader
April 2023

# Disclaimer

This presentation (this "**Presentation**") has been prepared by Zura Bio Limited, together with its affiliates (the "**Company**") and is being furnished to certain potential invest
Presentation is only intended for the recipient and may not be reproduced or redistributed without the prior written consent of the Company. This Presentation is not and may not be relie
legal, tax or investment advice and does not constitute an offer to sell or a solicitation of any offer to buy an interest in the Company. An investment in the Company will only be made
private negotiation and the definitive transaction documents. Each prospective investor should consult its own attorney, business adviser, and tax adviser as to legal, business, tax and relate
information contained in this Presentation.

This Presentation is provided for informational purposes only and contains proprietary and confidential information of the Company. The recipient of this Presentation shall kee
its contents confidential, shall not use this Presentation and its contents for any purpose other than as expressly authorized by the Company and shall be required to return or d
Presentation or portions thereof in its possession promptly following request for the return or destruction of such copies. By accepting delivery of this Presentation, the recipient is
foregoing confidentiality requirements.

Neither the Company nor any of their affiliates or their respective employees, directors, officers, contractors, advisors, members, managers, successors, representatives or agents
or warranty as to the accuracy or completeness of this Presentation, and shall have no liability for any representations or warranties (expressed or implied) contained in, or for any omissio
Presentation or any other written or oral communications transmitted to the recipient in the course of its evaluation of a potential investment in the Company. Only those represe
contained in a definitive agreement with the Company shall have any legal effect.

The information in this Presentation includes forward-looking statements. All statements other than statements of historical fact are forward-looking statements. The words "assur
"expect," "forecast," "intend," "may," "model," "plan," "potential," "project," "should," "variable," "will," "would," and similar expressions are intended to identify forward-looking statemer
statements in this Presentation relate to, among other things, future events involving, or future performance of, the Company, including the results of preclinical testing and clinical tria
Company to receive necessary regulatory approvals. The forward-looking statements are based on assumptions and analyses made by the Company in light of its experience and percep
current conditions, expected future developments, and other factors that it believes are appropriate under the circumstances. These statements are subject to numerous known
uncertainties which may cause actual results to be materially different from any future results or performance expressed or implied by the forward-looking statements, including adv
conditions and financing risks. Some of the forward-looking statements in this Presentation relate to events or developments anticipated to occur numerous years in the future, which incr
actual results will differ materially from those indicated in such forward-looking statements. The forward-looking statements and other information in this Presentation are presented as
Company disclaims any commitment to update or revise the forward-looking statements set forth herein, whether as a result of new information, future events or otherwise, except as may b
law.

The Company reserves the right, at any time, to negotiate with one or more interested investors or to enter into an agreement with respect to, or to determine not to proceed with
prior notice to any other interested investors. The Company reserves the right to terminate, at any time, and for any or no reason, further participation by any investor and to modify any other

The Company recently completed a business combination ("**Business Combination**") with JATT Acquisition Corp ("**JATT**"). Following the Business Combination, the Company's secu
under the symbols "ZURA" and "ZURAW." Additional information about the Company, including risk factors and financial statements, is included in the Company's public filings available on
at www.sec.gov. You should carefully review the Presentation and the Company's public filings, and perform your own due diligence, prior to making an investment in the Company.

Investment in the securities described herein has not been approved or disapproved by the United States Securities and Exchange Commission (the "**SEC**"), or any other regulat
authority passed judgment upon or endorsed the merits of securities or the accuracy or adequacy of the information contained herein. Any representation to the contrary is a criminal offens

# Investment Highlights

**Experienced and proven leadership**

- Experienced drug developers and asset hunters led by ex-Arena leaders
- Product approvals & commercialization
- Significant corporate transactions

**Multiple Phase 2 programs**

- Validated mechanisms pursuing innovative new development paths
- Potential Best in Class attributes combined with strategic clinical development to enhance differentiation

**Track Record of Execution**

- Deep relationships with KOL community
- Prior CRO leadership history within team enhances our Sponsor status
- Recent precedent of on-time execution in crowded I&I spaces (UC, AD, etc.) includes absorbing COVID impact without delays

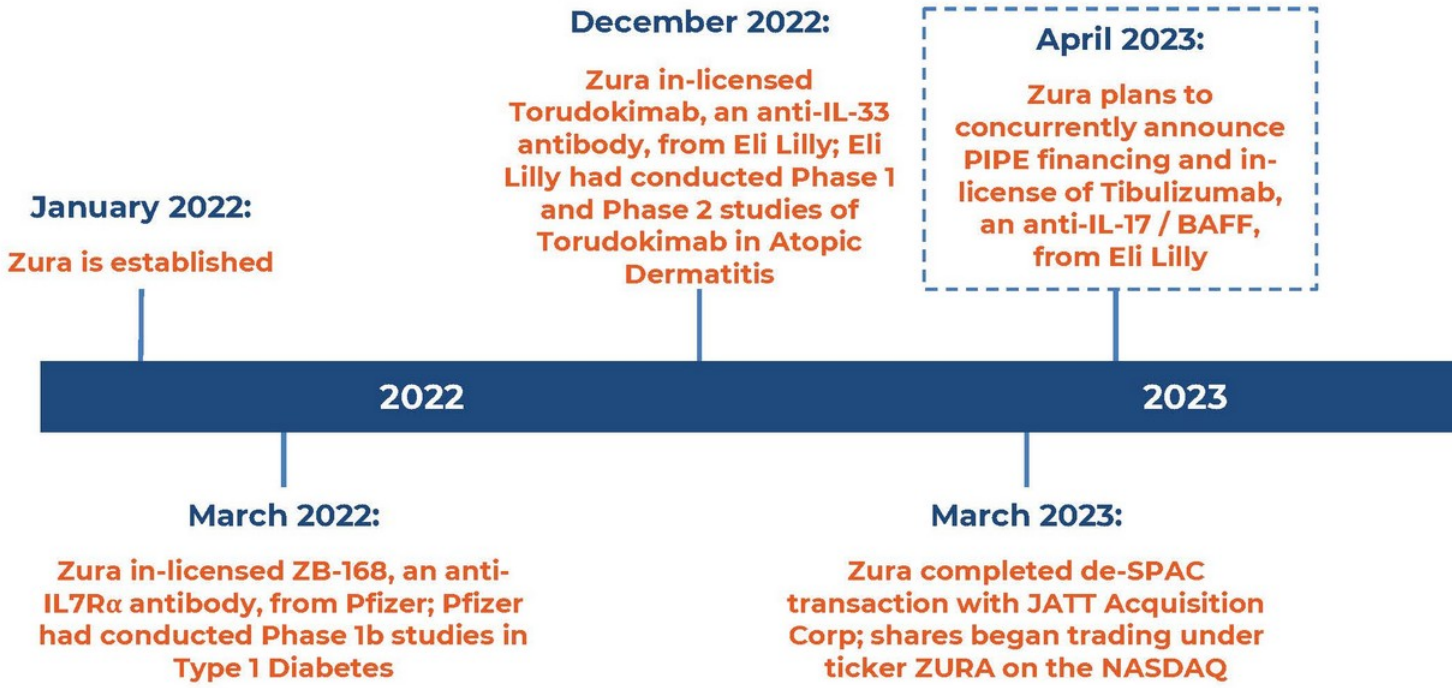
**Strong and committed financial backing with long-term alignment**

- Investors aligned with long-term commitment
- Successful PIPE transformation, including $65M in funding through Business Combination

Abbreviations: AD, Atopic Dermatitis; CRO, Contract Research Organization; KOL, Key Opinion Leader; UC, Ulcerative colitis

Note: please see language in the Disclaimer regarding 'forward-looking statements'

# Zura Company Timeline



# An Experienced Leadership Team from A to Z

**Amit Munshi**
Chairman

ARENA PHARMACEUTICALS
EPIRUS
PERCIVIA
AMGEN

**Someit Sidhu M.D.**
Chief Executive Officer and Director

McKinsey & Company
IZANA BIOSCIENCE
JATT
PATHIOS THERAPEUTICS

**Chris Cabell M.D.**
Chief Medical Officer and
Head of Research and Development

ARENA PHARMACEUTICALS
QuintilesIMS
PULMATRIX
emergent

**Kim D**
Chief Lega

kaléo
AMG

**Verender Badial**
Chief Financial Officer

JATT
SOCIETE GENERALE
RBS
Rothschild & Co
ABN·AMRO

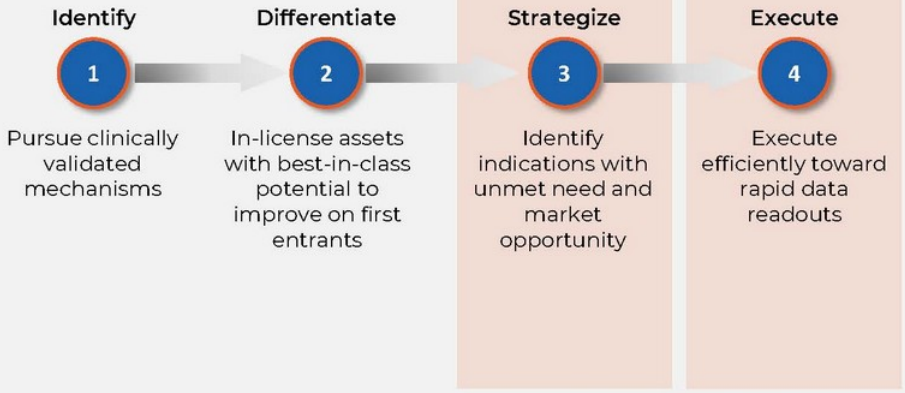
**Mike Howell Ph.D.**
Chief Scientific Officer and
Head of Translational Science

DermTech
MedImmune
Incyte
Boehringer Ingelheim

**Gary Whale Ph.D.**
Chief Technology Officer

emergent
EUSAPharma

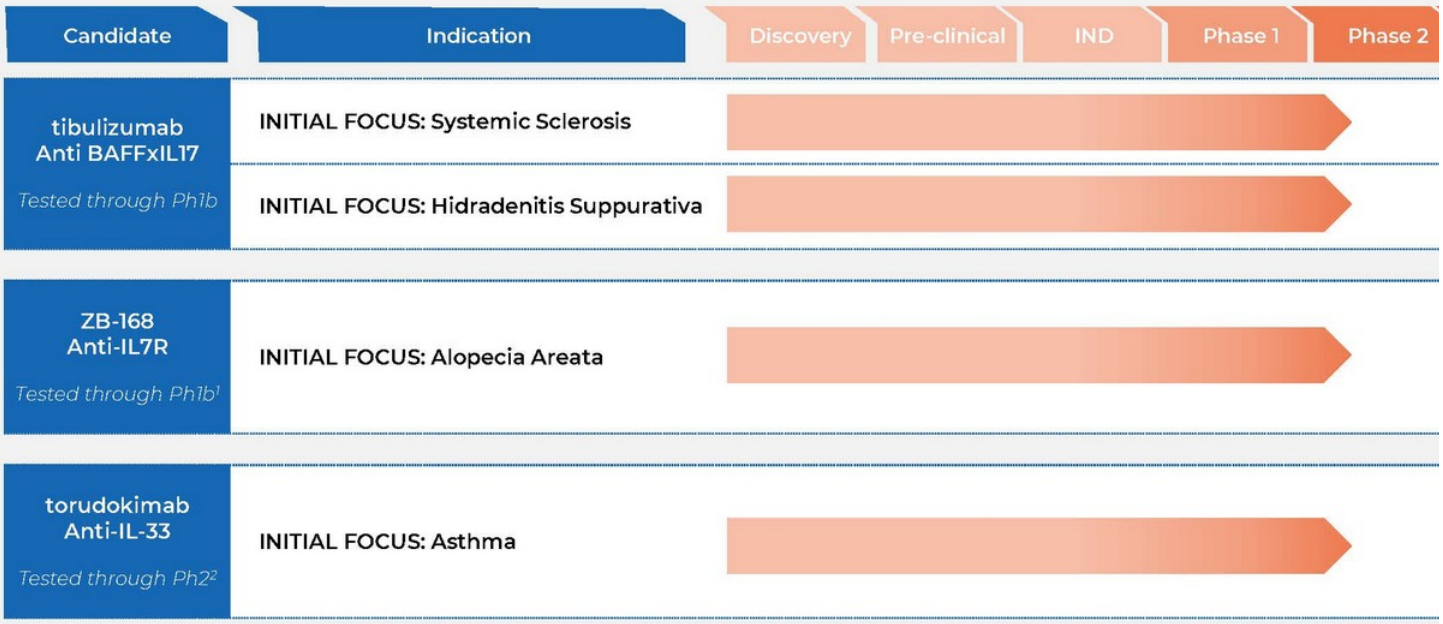
# Zura's Business Development Aligns with its Philosophy of Developing Validated Mechanisms in Novel Ways




Note: please see language in the Disclaimer regarding 'forward-looking statements'

# Clinical stage pipeline targeting key immunology pathways

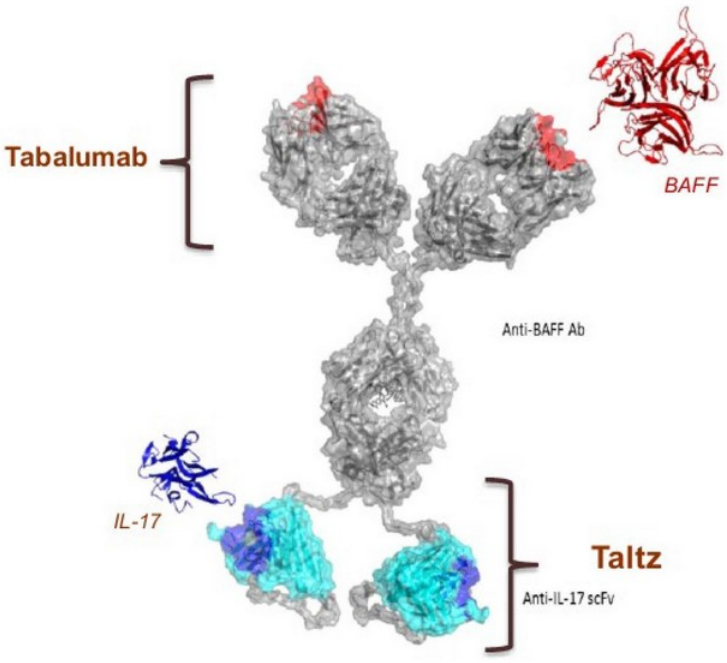
## Current financing will bring in ZB-106 as lead asset into Zura




Note: Clinical development plan subject to confirmation, pending regulatory and further clinical feedback

1. Herold et al. 2019. JCI Insight, 2. Laquer et al. 2022. Br J Derm

# Tibulizumab (ZB-106) is a Potential First-in-Class, Dual Antag Combining tabalumab and ixekizumab (TALTZ®)




**ZB-106 is an IgG-scFv engineered by the fusion of ixekizur and tabalumab[1,2]**

- ZB-106 neutralizes IL-17A or BAFF regardless of whether th are occupied
- ZB-106 binds in the same way as Taltz and tabalumab wit of binding sites
- Activity is mediated through direct target engagement ar
- Terminal half-life ~26 days

**Robust existing clinical and non-clinical data package**

- Two Phase 1b studies completed by Eli Lilly (RA and Sjögr
- 78 subjects have been dosed with ZB-106
  - 57 subjects = single dose; 21 subjects = multiple dose up
- Chronic toxicity studies completed with no adverse findin

**Durable and deep IL-17 and BAFF signaling blockade obse cutaneous dosing every 4 weeks**

- At target Q4W doses BAFF and IL-17 achieve maximum re

**Low rate of immunogenicity**

- Across 78 subjects exposed to ZB-106, only 1 subject teste drug Antibodies (ADAs)

**Safety profile to date appears to be consistent with ixekiz and IL-17A class**

1. Liu et al. 2016. *J Inflam Research*; 2. Manetta et al. 2014. *J Inflam Research*; 3. Benschop et al. 2019. MAbs

# Eli Lilly Deal Terms

## Terms of Tibulizumab (ZB-106) License

**Upfront:**

- Mid-teens upfront cash payment for exclusive global license

**Milestones:**

- Single digit development milestones
- Back-end milestones triggered at approval and sales-based
- Single to low double-digit royalties on net sales

**Other Key terms:**

- No development in select indications (a) plaque psoriasis, (b) pediatric psoriasis, (c) genital psoriasis, (d) p arthritis, (e) ankylosing spondylitis, (f) non-radiographic axial spondylarthritis, (g) chronic spontaneous ur and (h) juvenile idiopathic arthritis
- Right of first negotiation for Lilly upon completion of Phase 2b data
- Most patents expire in April 2033, but US patent expires June 2034
- Data protection is expected from marketing approval for 12 (US), 10 (EU), and 8 (JP) years

# Clinical Development

## Upcoming milestones

### tibulizumab (BAFFx17)

- 2 clinical studies for ZB-106
- Initiate phase 2 study in **Systemic Sclerosis** (2024)
- Initiate phase 2 study in **Hidradenitis Suppurativa** (2024)

### ZB-168 (IL-7Rα)

- Advance CMC program for ZB-168 ready to initiate clinical drug product at scale (H1 2024)
- Enable targeted launch of clinical trials in H2 2024 pending expected **phase 2 external catalysts in Ato Dermatitis, Ulcerative Colitis and Sjögrens Syndrome**

### torudokimab (IL-33)

- Gain FDA Regulatory feedback and alignment for torudokimab on phase 2/3 designs in Asthma (H2 202
- Enable launch of clinical trials in H2 2024 pending expected **phase 2 and 3 external catalysts in Asthm COPD**


ZE
Potential First-in-Class, Dual Ant
Combining tabalumab an
Note: please see language in the Disclaimer regarding 'forward-looking statements'

# IL-17 and BAFF Approved in Multiple Autoimmune Diseases

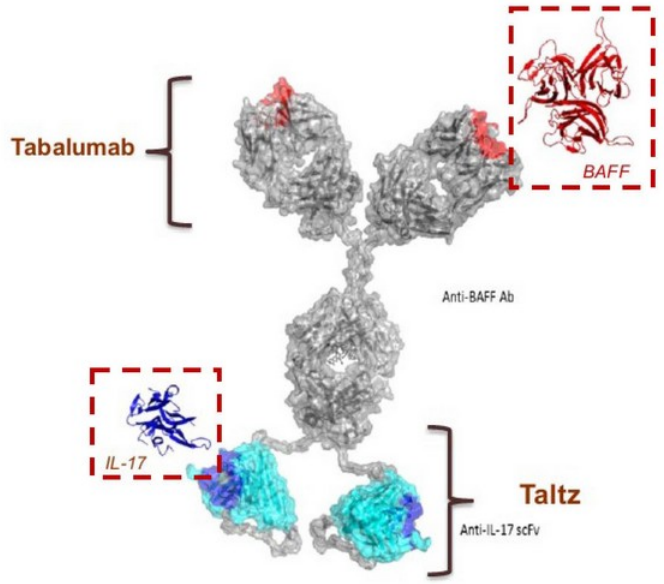
- **IL-17 and B-cell assets are widely recognized to have significant value**
- **ZB-106 represents an opportunity to pioneer a new approach to treating autoimmune diseases by directly addressi of immune inflammatory response**

| | | IL-17 | | | | IL-17 / BAFF | BAFF / TACI / API | | |
|---|---|---|---|---|---|---|---|---|---|
| | Company | NOVARTIS | Lilly | ACELYRIN | MoonLake | zurabio | GSK | RemeGen | CHIN |
| | Asset | Cosentyx (secukinumab) | Taltz (ixekizumab) | Izokibep | Sonelokimab | ZB-106 | Benlysta (belimumab) | Telitacicept | BION |
| | MoA | IL-17A | IL-17A | IL-17A/A | IL-17A/F | IL-17A / BAFF | BAFF | TACI fc | APF |
| | Delivery | SC / IV | SC | SC | SC | SC | SC / IV | SC | SC |
| Indications | Plaque Psoriasis | Approved | Approved | | Ph3 | | | | |
| | Psoriatic Arthritis | Approved | Approved | Ph2b/3 | Ph2 | | | | |
| | AS | Approved | Approved | Ph3 | | | | | |
| | SLE / Lupus | | | | | | Approved | App. China | |
| | HS | Filed | | Ph2b/3 | Ph2 | Ph2 Ready | | | |
| | Lupus Nephritis | Ph3 | | | | | Approved | | |
| | Sjögren's | | | | | | | Ph3 | |
| | IgAN | | | | | | | Ph2 | Ph |
| | Other | | | Uveitis (Ph2b/3) | | Syst. Sclerosis (Ph2 Ready) | Syst. Sclerosis (Ph2) | MG (Ph3) RA (Ph3) | |

Sources: Clinical Trials, Company Presentations, Wall Street Research and Evaluate Pharma.

# ZB-106 is a Combination of Two Compounds that have I Demonstrated Efficacy with an Established Safety Prof

- Taltz® (ixekizumab) is an approved anti IL-17 therapy with estimated peak sales >$3bn
- tabalumab is an anti-BAFF which has shown efficacy in some phase 3 trials




**TABALUMAB**

- 4,275 subjects dosed a studies
- Statistically significant a phase 3 study in SLE
- Demonstrated safety p

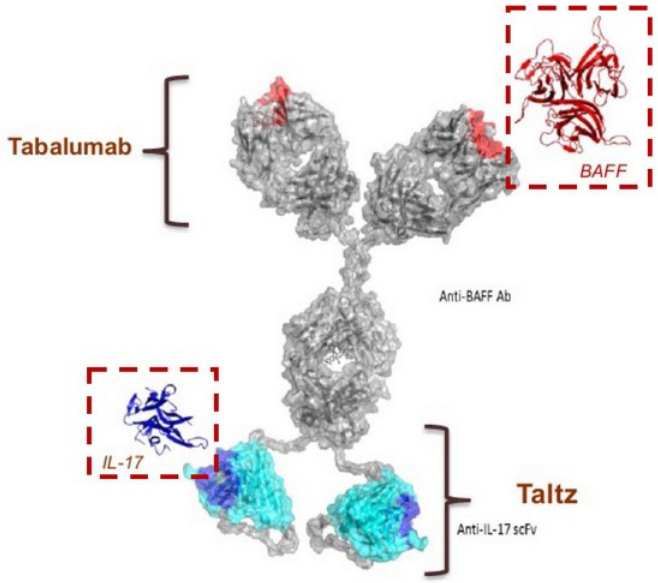
**IXEKIZUMAB (TALTZ®)**

- Commercially approve >$2.2bn of annual sale
- Demonstrated efficacy indications
- Demonstrated safety p

1. Eli Lilly Annual Report

# ZB-106 Has Broad Potential Therapeutic Applications

- Potential to be a first-in-class biologic in a number of autoimmune diseases where both BAFF and IL-1 implicated in the pathology[1,2]




**BAFF**

- **Systemic Sclerosis**
- Sjögren's Syndrome
- Systemic Lupus Erythema

**IL-17**

- **Hidradenitis Suppurativa**
- Uveitis
- Bechet's Disease
- Lichen Planus
- Pustular Psoriasis
- Impetigo Herpetiformis
- Pityriasis Rubra Pilaris

1. Kaegi et al. 2020. Allergy; 2. Wu and Dao, 2022. JDermTreat

Note: please see language in the Disclaimer regarding 'forward-looking statements'

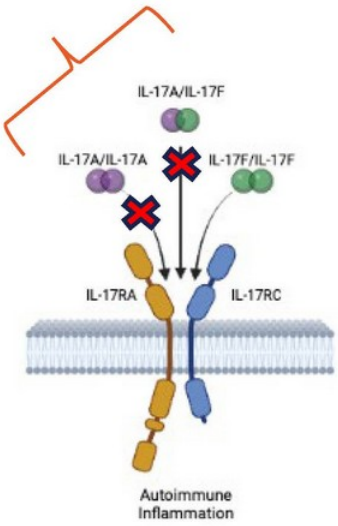
# ZB-106 Disrupts IL-17 and/or BAFF-Mediated Inflammation

**ZB-106 has the potential to treat diseases driven by B-cell and T-cell signaling**

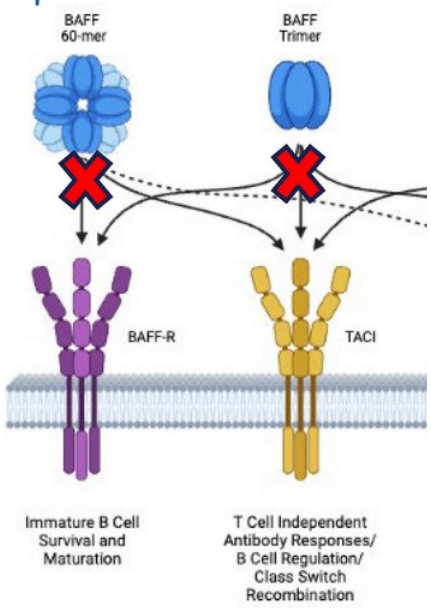
### T-cell and B-cell synergy

- Multiple T-cell driven diseases remain sub-optimally treated despite the growth in "pure play" anti-IL-17 drugs
- B-cell driven diseases often have a T-cell driven autoimmune component contributing to the pathology
- Combined approach to address T-cell and B-cell drivers of autoimmunity has the potential to increase clinical benefit

**IL-17**
**Binds to IL-17A preventing IL-17A/A and IL-17A/F heterodimerization[1]**




**BAFF**
**Binds to BAFF trimer and BAFF 60-mer preve**
**BAFF-R, TACI, and BCMA[2]**

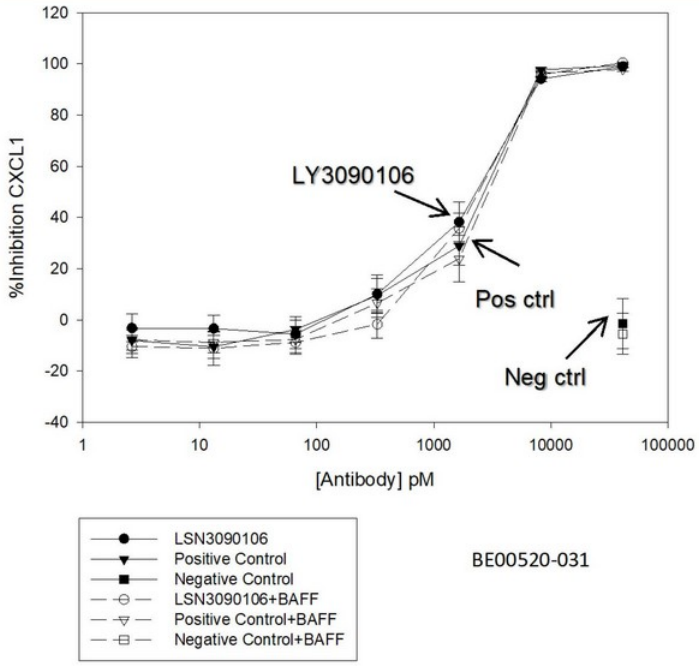



1. Liu et al. 2016. J Inflam Research; 2. Smulski and Eibel. 2018. FrontImmunol

Figure Ge

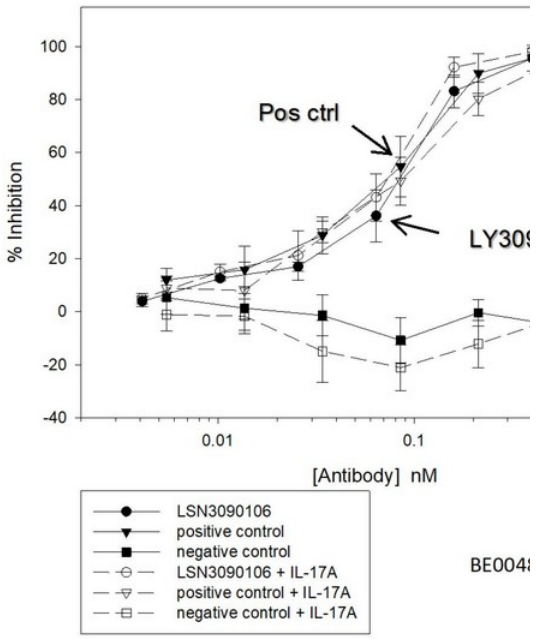
# ZB-106 (LY3090106) Independently Neutralizes IL-17 or BAFF

**ZB-106 inhibits IL-17 mediated CXCL1 production in HT-29 epithelial cells in a BAFF independent manner[1]**




BE00520-031

**ZB-106 inhibits BAFF-mediated proliferation i an IL-17 independent manner[1]**



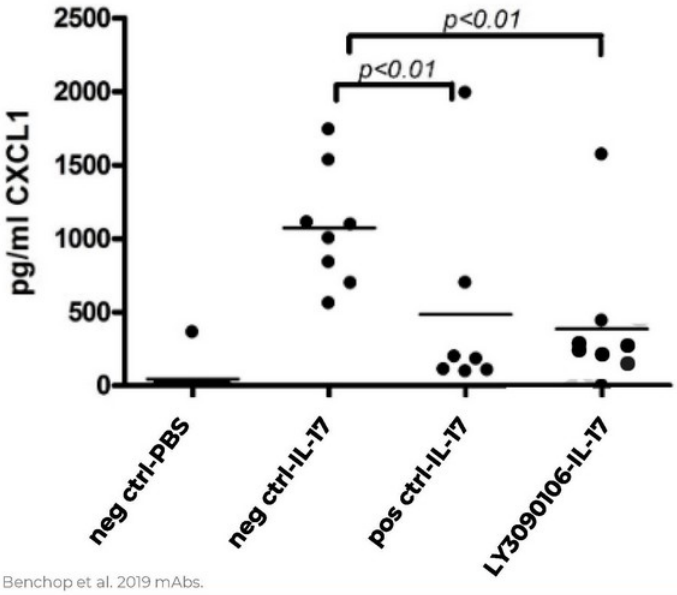

BE004

Benchop et al. 2019 mAbs.

# ZB-106 (LY3090106) Inhibits IL-17 or BAFF-Mediated Inflamm

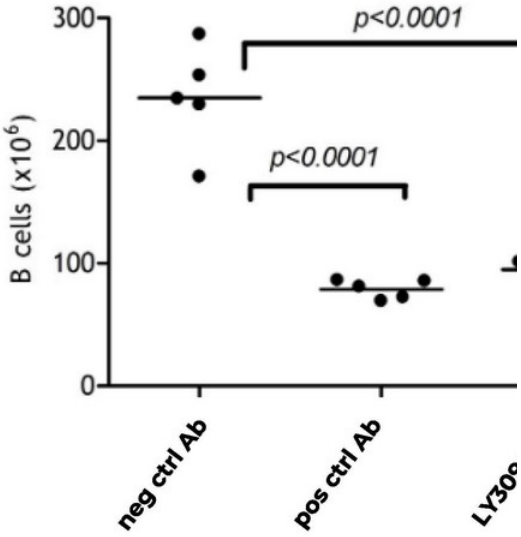
**ZB-106 inhibits IL-17 mediated CXCL1 production in C57Bl/6 mice similar to ixekizumab (positive control)[1]**

**IL-17-induced CXCL1 Levels In-Vivo**




**ZB-106 reduces total B cell counts in the spleen transgenic mice similar to tabalumab (pos**

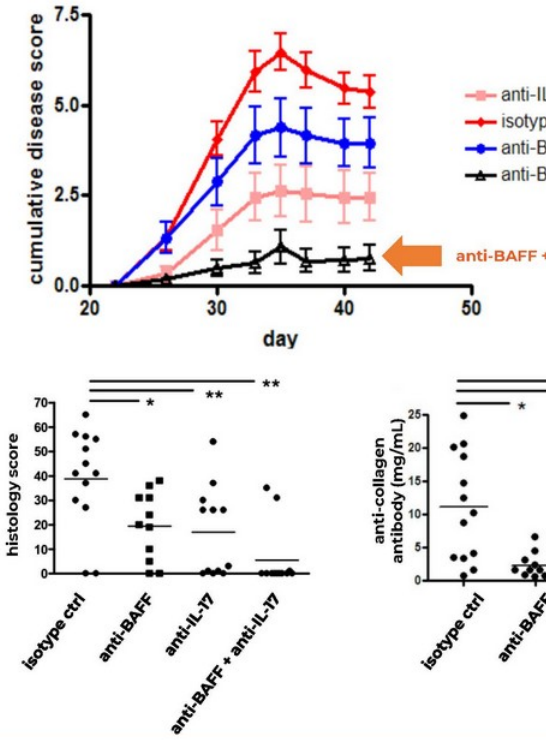
**Total B Cells**




Benchop et al. 2019 mAbs.

# Combining IL-17 and BAFF Neutralization in a Murine Model Arthritis Enables Improvement in Therapeutic Benefit

- Rheumatoid arthritis is a prototypic autoimmune disease where individually targeting IL-17-mediated inflammation or depleting B cells has been clinically validated
- The collagen-induced arthritis (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**
  - **Inflammation in the hind paw (histology score)**
  - **Anti-collagen antibodies**



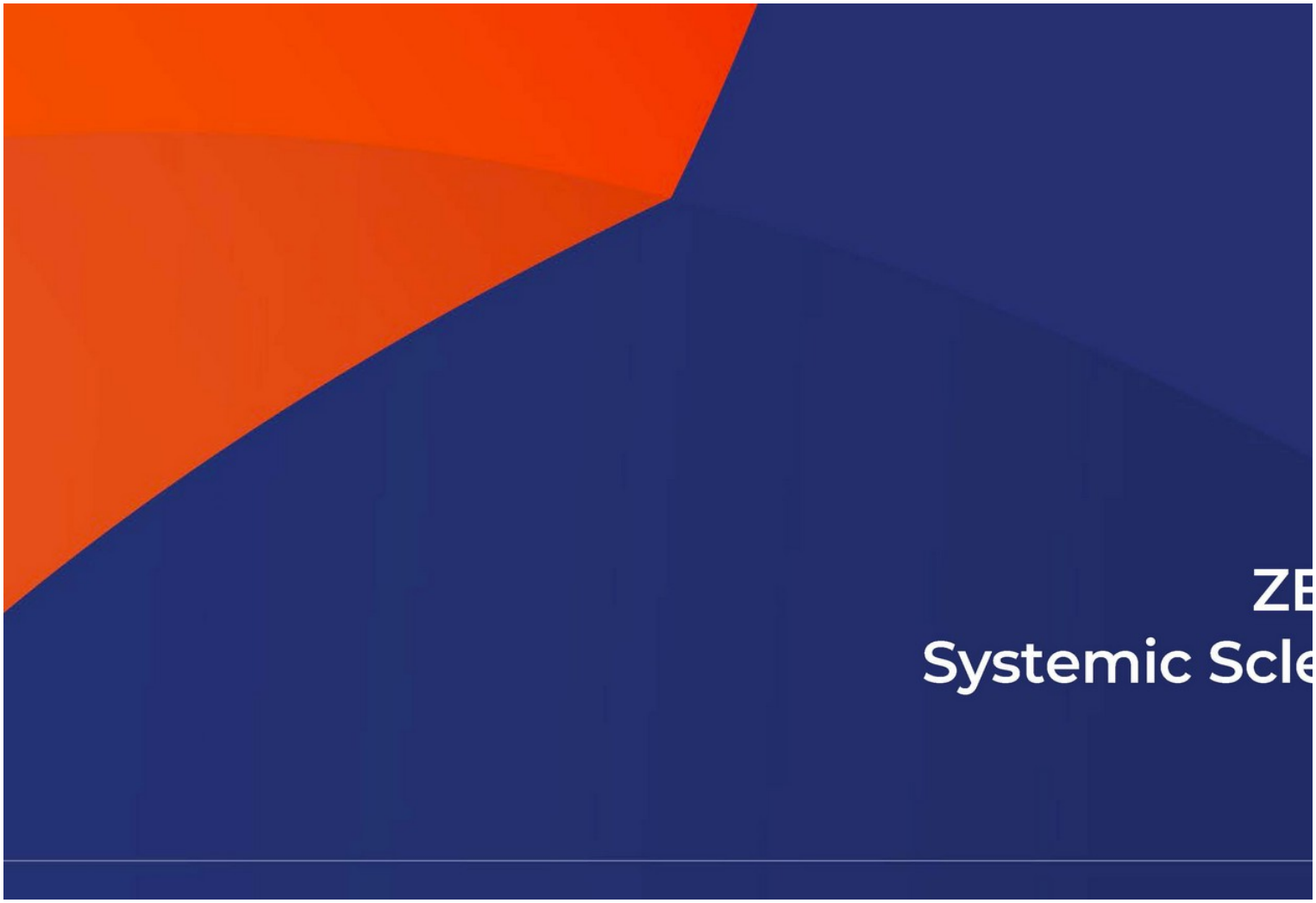

Source: Zura Internal Data, IND Briefing

# ZB-106 is Clinically De-Risked Through P1b
# 78 Subjects/Patients Dosed Across 3 P1/1b studies

| Pharmacokinetics | Pharmacodynamics | Safety and AE |
|---|---|---|
| • $t_{1/2}$ is 26.9 days<br>• Bioavailability after SC doses was 62.9%<br>• 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 | • In Ph1b healthy volunteer study in RA patients there was multiple impacts on PD markers<br>• Decrease in CD20+ B-cells with higher doses generally associated with larger changes from baseline<br>• Decrease in hs-CRP AUC was associated with higher ZB-106 AUCs | • SAD studies: No deaths or<br>• MAD study: No deaths, sir SAE of neutropenia with r<br>• Most frequent TEAE: Head transient neutropenia, na diarrhea<br>• No infections<br>• In the multiple ascending study, one subject had TE detected at a titer of 1:512( |
| **Established dosing regimen** | **Demonstrated PD in patients in ph1b** | **Safety / ADA pr line with Ta** |

**ZB-106 is a highly validated molecule that enables the opportunity to deliver on the promise of both I inhibition in autoimmune disease**

Source: Zura Internal Data, IND Briefing


ZE
Systemic Scle

# Overview of Systemic Sclerosis

## Disease Overview

- Systemic sclerosis (SSc) remains among the deadliest of the rheumatic diseases
- Patients with SSc often have severe disability, fibrosis-related organ failure, and die prematurely
  - Up to 50% develop interstitial lung disease (ILD), the most common cause of mortality in these patients
  - The disease has a severe impact on patients' lives, causing a variable constellation of symptoms including Raynaud's p arthritis, painful ulcers on the fingers and toes, thickening and scarring of the skin, shortness of breath, hypertension, fatigue

## Unmet Need

- High unmet need remains as standard of care relies on immunosuppression therapy and biologic agents which are toxi tolerated
  - Other current treatments only aim to manage symptoms and include pain relief through nonsteroidal, anti-inflamm medications or corticosteroids
- **Two disease-modifying drugs are approved for severe lung complications of the disease (SSc-ILD)**, but no effective t exists that combats the disease across organ systems

## Patient Population

- Varying prevalence estimates among world populations, with higher population estimates in the US than in Europe or A
- Data suggests ~250 per million adults in the US (80-100K patients), 233 per million in Australia (~6K patients), 88-158 per Western Europe
- Women are affected more frequently than men, with a female-to-male ratio of 5:1 and most commonly presents betwee 30-40 years

Source: Medscape, BMJ best practice

# Overview of Systemic Sclerosis Potential Opportunity

**Rare and life-threatening autoimmune disease characterized by tissue inflammation a**
**that has no disease modifying therapy**

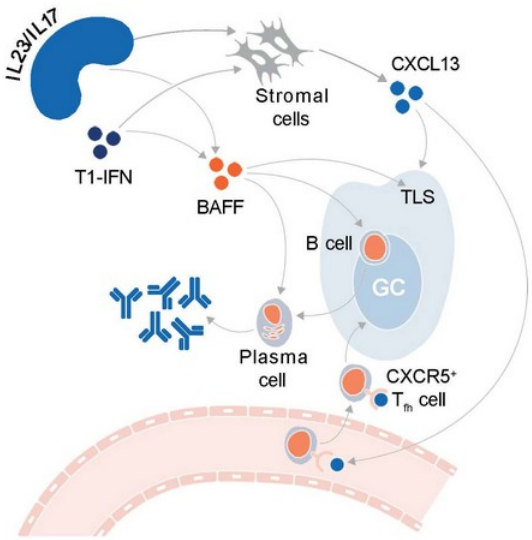
| ~200,000 | 40-60% | Zero | $2 |
|---|---|---|---|
| people with SSc in US, EU and Japan[1] | mortality in 10 years[2] | SSc-specific drugs approved | annual market o |

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 b
5. Internal assumption based on demand research and rare disease analogues

# IL-17 and BAFF Inhibition Pathways Have Shown Efficacy in Place Controlled Trials in Systemic Sclerosis (SSc)

## IL-17 efficacy in SSc

- Brodalumab treatment in SSc leads to improved clinical outcomes[1]
- IL-17 known to play key role in the fibrotic process of various organs like lung, kidney, heart and skin
- Th17 cell–derived IL-17 was significantly higher in the skin and serum of SSc patients[2]




## Role of BAFF i

- Belimumab t efficacy in op and one singl study[3]
- Phase 2/3 init by GSK
- SSc patients h abnormalities by chronic hy of memory B
- BAFF and aut are key bioma

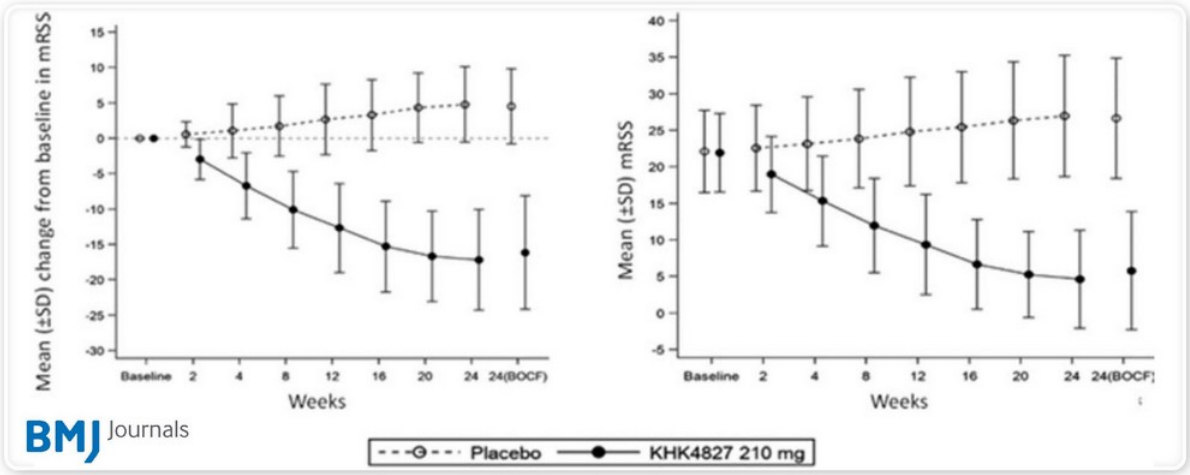
**ZB-106 has the potential to treat the TH17 and BAFF components of SSc**

1. Fukasawa et al. 2022. AnnalsRheumDisease; 2. Yang et al. Arthritis Research & Therapy 2014 3. Ebata et al. 2021. Lancet Rheumatol 4.Sato et al. 2004. MolImmunol.; 5. Senecal et al 2020. JSclerodermaRelatDisord; 6. Sato et al. 2000. JImmunol.

# Brodalumab Treatment in SSc has Demonstrated Improved Clinical Outcomes

- Brodalumab achieved the primary endpoint (treatment difference of least square mean: −21.2 [95% CI -2
  P<0.0001), and demonstrated a **rapid, sustained reduction in mRSS over 52 weeks**[1]
- The outcome of brodalumab treatment suggested its therapeutic effects on lung/respiratory functions,
  the symptoms of gastroesophageal reflux disease, and QOL without any noteworthy safety concerns

**mRSS over the 24-week follow-up (Mean +/- SD)**




Source: Fukasawa et al. 2022. AnnalsRheumDisease

zurabio

# Belimumab Treatment in SSc has Demonstrated Improved Clinical Outcomes

## Overview of Belimumab in SSc

- 52-week, investigator initiated, single center, double blind, placebo-controlled pilot study
- 20 subjects with dcSSC on MMF treated with belimumab or placebo
- No significant differences in AEs between belimumab group and placebo
- Patients in both treatment groups experienced clinical improvements in MRSS favoring belimumab (p=NS)
- All secondary endpoints favored belimumab with statistical significance in 2 endpoints: SHAQ DI and VAS Raynaud's phenomenon
- GSK recently received Orphan Drug Designation for the potential treatment of SSc with plans to initiate a phase 2/3 trial in SSc-ILD in 1H 2023

**Table 2.** Change in primary and secondary end points at

| | Belimumab + MMF (n = 9) | Placeb |
|---|---|---|
| MRSS, 0–51 | −10 (−13, −9) | −3.0 ( |
| SHAQ DI score, 0–3 | −0.25 (−0.38, −0.25)† | 0.00 ( |
| VAS pain score, 0–150 mm | −10.5 (−40.5, 6.5) | −1.0 ( |
| VAS RP score, 0–150 mm | −30.0 (−40.0, −14.0)‡ | 0.0 ( |
| VAS ulcers score, 0–150 mm | −12.0 (−38.0, 1.0) | 0.0 ( |
| VAS breathing score, 0–150 mm | 2.0 (0.0, 7.0) | 0.0 ( |
| VAS overall score, 0–150 mm | −14.0 (−29.0, −9.00) | −10.0 ( |
| SF-36 MCS score, 0–100 | 7.50 (2.50, 18.50) | 3.00 ( |
| SF-36 PCS score, 0–100 | 8.00 (−3.50, 19.00) | −3.00 ( |
| PGA, 0–10 | −4.43 (−8.05, −0.90) | −1.67 ( |
| FVC, % predicted | 5.00 (0.00, 8.00) | −2.00 ( |
| DLco, % predicted§ | 2.00 (−7.00, 7.00) | 0.00 ( |
| CRISS score | 0.61 (0.34, 0.88) | 0.03 ( |

* Values are the median (interquartile range). MMF = late mofetil; CRISS = composite response index in diffus systemic sclerosis (see Table 1 for other definitions).
† $P = 0.042$ versus placebo + MMF.
‡ $P = 0.029$ versus placebo + MMF.
§ Adjusted for hemoglobin level.

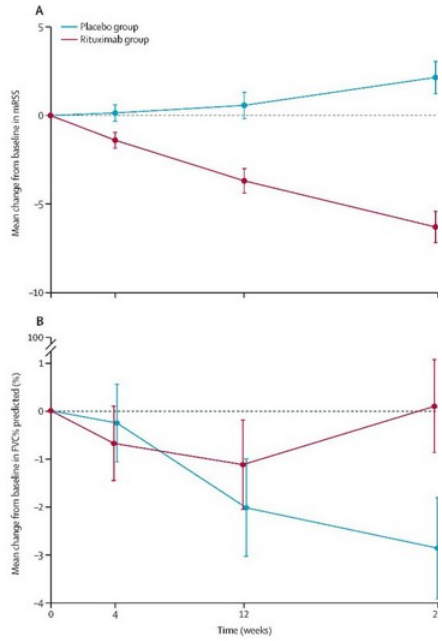
Source: Gordon et al..2018. ArthRheumatol.

# B-Cell Depletion Therapy with Rituximab in SSc has Demonstrate Improved Clinical Outcomes

## Rituximab in SSc shows efficacy

- Multiple Studies have shown the potential effectiveness of Rituximab in SSc – mainly open label and observational studies
- The most compelling data come from the DESIRES double blind – placebo controlled trial[1]
  - Fifty-six patients with SSc entered the study
  - The primary endpoint of mRSS change after 24 weeks of study treatment
  - Rituximab -6.30 points vs. PBO +2.14 points ($p < 0.0001$)
  - 48 / 56 subjects had SSc-ILD 2.96% FVC improvement at 24 weeks vs. PBO ($p=0.04$)

## Randomized data shows improvemer SSc-ILD

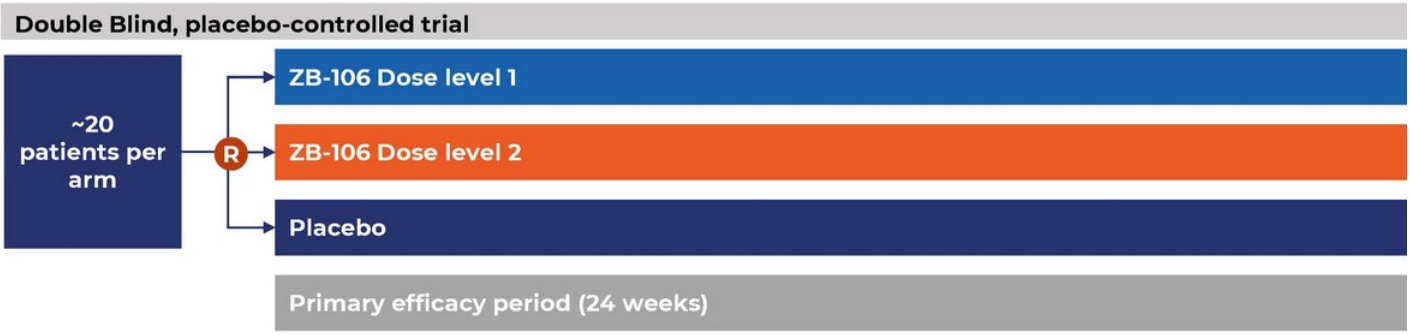



Source. Ebata et al. 2021. Lancet Rheumatol

# Proposed Phase 2 Trial Design

**Key inclusion criteria:**

- mRSS 10-29
- Subject presented the first symptoms of sclerosis other than Raynaud's phenomenon within 60 months before enrollme




**Key efficacy endpoints:**

- Change mRSS
- CRISS
- SHAQ DI
- VAS (RP, Pain, Ulcers, Breathing)
- FVC, DLCO
- PK / PD assessments

**Key safety endpoints:**

- General Safety and Tolerability
- Severe infection
- Neutropenia
- ADA / nAb

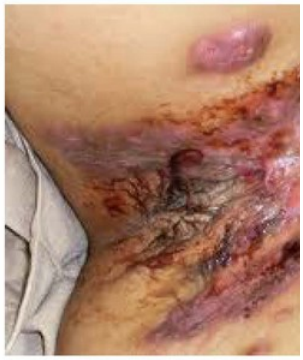
Note: Clinical development plans are subject to ongoing review, regulatory feedback


ZB-
Hidradenitis Suppur

# Overview of Hidradenitis Suppurativa

## 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

- Estimated that there are **~300K** people living with Hidradenitis Suppurativa in the U.S. (1-2% global prevalence)
- Average of 7 years to diagnose globally
- High unmet need as there is only **One FDA-approved treatment for Hidradenitis Suppurativa (Humira)**
  - Current treatments only aim to manage symptoms and include palliative care such as over-the-counter eye topical cyclosporine and off-label treatments such as steroids or immunosuppressants to manage systemic

1. Moran et al. JID 2017; 2. Banerjee et al. 2017. Immunol. Invest. ; 3. Sabat et al. JACI 2022; 4. Garg et al. 2017 JAMA Dermatol; 5. Ingram. 2020. BrJDermatol

# Overview of Hidradenitis Suppurativa Opportunity

## Despite Multiple IL-17 Development Programs, There is Significant Opportunity Unmet Need in HS

**First in Class Therapy With Transformational Potential**

- Known efficacy of IL17
- Strong rationale for BAFF
- Known dosing profile

**Large Addressable Market**

**~300K** Living U.S. Patients[1]

**1-4%** Global Prevalence[2]

**$** P r

**Significant Unmet Need**

**1 Drug** Approved

**Efficacy ceiling with IL17 alone**

*~10-20%*

HiSCORE 50 Placebo-Adjusted[4]

h ir re al ea of

1. Epidemiology of Hidradenitis Suppurativa: Prevalence, Pathogenesis, and Factors Associated with the Development of HSInge E. Deckers &Hessel H. van der Zee &Errol P. Prens 2. Eval
3. Jefferies Wall Street Research 4. Cosentyx and Bimzelx Public Presentations, Publications and Research

# Despite Multiple IL-17 Development Programs, There is Sign Opportunity to Address Unmet Need in HS

**1 IL-17 A/F hypothesis still remains to be proven in the clinic**

- IL-17 mediated inflammation is a key driver of pathophysiology in HS
- Multiple IL-17 compounds have shown efficacy, however, there were minimal differences between therap 17A alone versus those targeting IL-17A/F

**2 Smaller therapeutics may not achieve higher efficacy or convenience**

- Izokibep (IL-17A/A blocking peptide) reported improvement in a small open label study that enrolled HS p classified as Hurley Stage 2
- Data presented were similar to secukinumab Ph2 open label study in HS suggesting additional studies a address the role of tissue penetration and smaller therapeutic approach

**3 Despite clinical validation of IL-17, there remains a significant therapeutic gap for large number of pat**

- HiSCR50 at 16 weeks tends to be ~ 15-30% (PBO adjusted), leaving substantial unmet need with opportun differentiated therapy
- Addition of B-cell targeted therapies has the potential to improve overall clinical response compared wit

**ZB-106 may address the efficacy gap raised for current IL-17 approaches in HS**

Sources: Company Presentations, Publications and Research.

# Public Data in Multiple P3 Studies Shows IL-17 is Clinically Validated Pathway to Treat HS

**Recent HS Data**

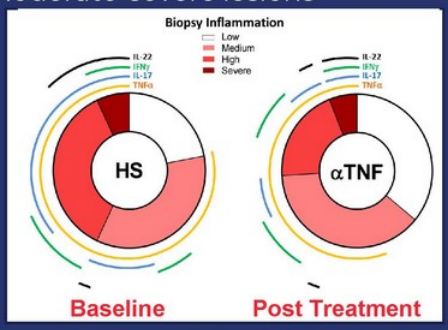
| Company (Asset) | | abbvie Humira | NOVARTIS Cosentyx | ucb Bimzelx | A |
|---|---|---|---|---|---|
| Mechanism | | TNF-α | IL-17A | IL-17A/F | |
| Administration | | SC | SC / IV | SC | |
| Phase | | PIONEER I & II Phase 3 | SUNSHINE & SUNRISE Phase 3 | BE HEARD I & II Phase 3 | Phase |
| Dosing | | 40mg QW for 12W | 300mg Q2W for 16W | 320mg Q2W for 16W | 160m |
| Total Patients | | n=633 | n=360 | Est. n=579 | |
| Efficacy (HiSCR50) | Non-Placebo Adjusted | 42% - 59% at W12 | 42% - 45% at W16 | 48% - 52% at W16 | |
| | Placebo-Adjusted | 16% - 31% at W12 | 11%+ at W16 | 19% - 20% at W16 | |
| Safety / Tolerability | Most Common AEs | Headache 9% - 13% at W12 | Headache 9% - 12% at W16 | Hidradenitis 7% - 9% at W16 | Injecti |
| | Candidiasis | 0% at W12[1] | 0% - 3% at W12[1] | 4% - 7% at W16 | |

Sources: Company Presentations, Publications and Research.
1. Represents data from psoriasis trial. 2. Represents safety data from psoriatic arthritis trial.

# Limitations of Current Approaches in HS

## Scratching the Surface

- Treatment with anti-TNFα therapy fails to downregulate inflammatory cytokines (IL-22, IL-17, IFNγ) in moderate-severe lesions[1]




- The presence of dermal tunnels increased the amount of time needed to achieve HiSCR50 with adalimumab[2]

## Tunnelling into HS

- Recent literature highlights the role of dermal tunnels in t pathogenesis of HS[2,3]
- Dermal tunnels in HS are characterized by increased cellu including neutrophils; and Sabat et al. demonstrated incre production by neutrophils[3]
- Transcriptomic profiling highlights increased IL-17A and E expression in dermal tunnels[3,4]
- Dermal tunnels were additionally shown to have increase B cells[3] and B cell targeting therapies are currently under in HS[6]
- One significant drawback of the HiSCR is the lack of a dyn measurement of draining tunnel; therefore, not fully capt anti-inflammatory properties of a therapeutic
- The International Hidradenitis Suppurativa Severity Score (IHS4) was developed to assess inflammatory nodules (1 p abscesses (2 points) and draining tunnels (4 points)

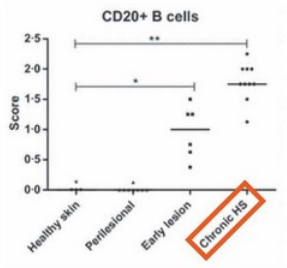
1. Moran et al. JID 2017; 2. Frew et al. 2021 Clin Exper Derm; 3. Sabat et al JACI 2023; 4. Gudjonsson et al. 2020; 5. Carmona-Rivera et al. JID 2022; 6. https://clinicaltrials.gov/ct2/show/NCT038

# Addition of BAFF has Potential to Provide Superior Efficacy to IL-17 Alon

## B-cells in HS lesions

- HS lesions have increased numbers of CD20+ B and CD138+ Plasma Cells[1]
- B-cell activating factor (BAFF) is produced by B cells, macrophages, dendritic cells, and neutrophils
- BAFF regulates B-cell survival, maturation and differentiation

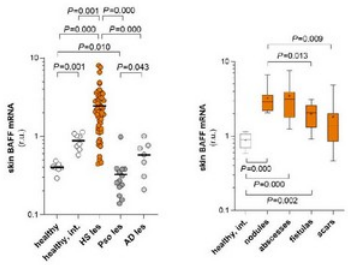
**CD20+ B cells in HS Lesions**




## BAFF in HS

- Increased BAFF expression in HS lesions[2,3]
- Lesional upregulation of BAFF and BAFF receptors is attributed to B cells and plasma cells[2,4]
- Neutralization of BAFF with a soluble variant of BAFF-R in HS lesional explants reduced the expression of key genes associated with B and plasma cell function[2]

**BAFF gene expression in HS**




## Clinical dat

- B cell depletion with ritu therapeutic benefit[5]
- 4/5 cases report complet lesions[5]

**Rituximab in HS case**

| | Complete Remission | No Remission | |
|---|---|---|---|
| Number of Cases, n | 4 | 1 | HS |
| Female/Male (ratio) | 1/3 (1:3) | 1/0 (-) | Hur |
| Mean Age (range) | 46.2 (20.5) | 54 (-) | I |
| Risk Factors, n (%)[a] | | | II |
| Smoking History | 1/2 (50.0) | 1/1 (100.0) | Com |
| Overweight or Obese | 2/2 (100.0) | 1/1 (100.0) | RA |
| Family History of HS | 0/2 (0.0) | 1/1 (100.0) | + |
| HS History, n (%) | | | PV + |
| HS Location[b] | | | ICT |
| Inguinal + Back | 1/3 (33.3) | 0/0 (0.0) | |
| Inguinal + Abdomen | 1/3 (33.3) | 0/0 (0.0) | |
| Gluteal | 1/3 (33.3) | 0/0 (0.0) | |

*CAAMR*, chronic active antibody-mediated rejection; *DDD*, Dowling-Degos dis carpotarsal osteolysis; *PsO*, psoriasis; *PV*, pemphigus vulgaris; *RA*, rheumatoid
[a]Smoking, BMI, and family history of HS was not reported in 2/4 complete rem
[b]HS location was not reported in 1/4 complete remission cases and 1/1 no remi
[c]Hurley stage was not reported in 1/4 complete remission cases.

1. Van der Zee et al. 2012. Br J Derm; 2 Rumberger et al. 2020. J Inflam Research; 3.Sabat et al 2022. JACI; 4. Gudjonsson et al. 2020. JCI Insight.; 5. Seigel et al 2023. JCutanMedicSurgery

# Anti-CD20+ and Anti-BAFF Treatment in HS
# ZB-106 Therapeutic Potential Opportunity

## Rituximab in HS

- Chimeric mAb to CD20, upon binding triggers cell death
- Used off label in a range of autoimmune diseases
- Case reports in HS (systematic review 2023)[1]
  - Majority with complete remission when treated with Rituximab did not respond to previous therapy including antibiotics and surgical excision, antibiotics alone, and isotretinoin with benzoyl peroxide.

## Case report breakdown – 80% full remission[1]

**Supplementary Table 1.** Demographic and Clinical Features of Patients with HS Treated with Rituximab

| | Complete Remission | No Remission | | Complete Remission | No Remission |
|---|---|---|---|---|---|
| **Number of Cases, n** | 4 | 1 | **HS History (cont), n (%)** | | |
| **Female/Male (ratio)** | 1/3 (1:3) | 1/0 (-) | **Hurley Stage[c]** | | |
| **Mean Age (stdev)** | 46.2 (20.5) | 54 (-) | **I** | 2/3 (66.7) | 1/1 (100.0) |
| **Risk Factors, n (%)[a]** | | | **II** | 1/3 (33.3) | 0/1 (0.0) |
| **Smoking History** | 1/2 (50.0) | 1/1 (100.0) | **Comorbidities, n (%)** | | |
| **Overweight or Obese** | 2/2 (100.0) | 1/1 (100.0) | **RA** | 2/4 (50.0) | 0/1 (0.0) |
| **Family History of HS** | 0/2 (0.0) | 1/1 (100.0) | **+ PsO** | 0/4 (0.0) | 1/1 (100.0) |
| **HS History, n (%)** | | | **PV + DDD** | 1/4 (25.0) | 0/1 (0.0) |
| **HS Location[b]** | | | **ICTO + CAAMR** | 1/4 (25.0) | 0/1 (0.0) |
| **Inguinal + Back** | 1/3 (33.3) | 0/0 (0.0) | | | |
| **Inguinal + Abdomen** | 1/3 (33.3) | 0/0 (0.0) | | | |
| **Gluteal** | 1/3 (33.3) | 0/0 (0.0) | | | |

*CAAMR*, chronic active antibody-mediated rejection; *DDD*, Dowling-Degos disease ; *HS*, hidradenitis suppurativa; *ICTO*, idiopathic carpotarsal osteolysis; *PsO*, psoriasis; *PV*, pemphigus vulgaris; *RA*, rheumatoid arthritis
[a] Smoking, BMI, and family history of HS was not reported in 2/4 complete remission cases.
[b] HS location was not reported in 1/4 complete remission cases and 1/1 no remission cases.
[c] Hurley stage was not reported in 1/4 complete remission cases.

## Implications for ZB-106

- **CD20+ B-Cells**
  - ZB-106 has direct effect reducing CD20+ B
- **BAFF**
  - Increased BAFF expression in HS lesions[2,3]
  - Lesional upregulation of BAFF and BAFF r attributed to B cells and plasma cells[2,4]
  - Dysregulated BAFF expression contribute immune diseases via effects on abnormal activation, proliferation, survival, and imm secretion[5]
  - Murine models in RA provide evidence of activity of Anti-BAFF and Anti-IL-17
  - ZB-106 has been shown to have a clinical i diseases with elevated BAFF (e.g. SLE) wit decreases in B-cells and serum immunog
- **ZB-106 → Opportunity to improve clinical o**
  - Impacting CD20+ B-cells directly
  - Inhibition of abnormal B-Cell activation ar immunoglobulin secretion

Sources: 1. Seigel et al 2023. JCutanMedSurgery; 2. Rumberger et al. 2020. JInflamResearch; 3. Sabat et al 2022. JACI; 4. Gudjonsson et al. 2020. JCI Insight.; 5. Bosello et al 2007. IntJImmunc 6. Merrill et al. 2016. Ann Rheum Dis

# ZB-106 in Hidradenitis Suppurativa
# Clinical Development Plan Rationale

## Rationale to study HS: Opportunity for superior clinical response based upon IL-17 + BAFF inhibition

- IL-17 blockade in HS is a validated target with clear evidence of efficacy
- HiSCR50 at 16 weeks tends to be ~ 50% (placebo adjusted HiSCR50 ~15-30%), leaving substantial unmet
- Translation data indicate an interplay between B cells and the IL-17 pathway in HS
- Case reports have shown that rituximab has an impact on HS clinical course

## Dosing Rationale

- We have clear dosing windows for ZB-106
- ZB-106 clinical safety supports 6-fold “window” between max target engagement and max human dose

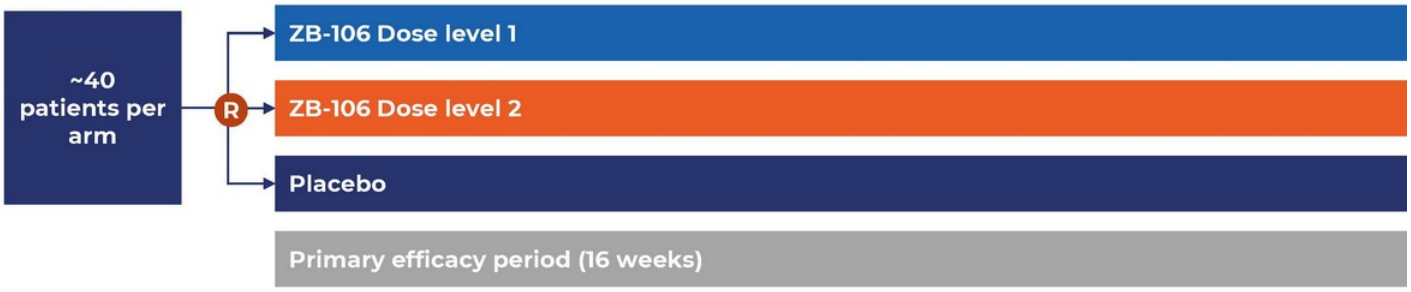
Source: Zura Internal Data

# Proposed Phase 2 Trial Design

**Key inclusion criteria:**

- Moderate to Severe HS
- Hurley Stage II/III
- Total abscess and inflammatory count (AN) ≥ 3

**Double Blind, placebo-controlled trial**



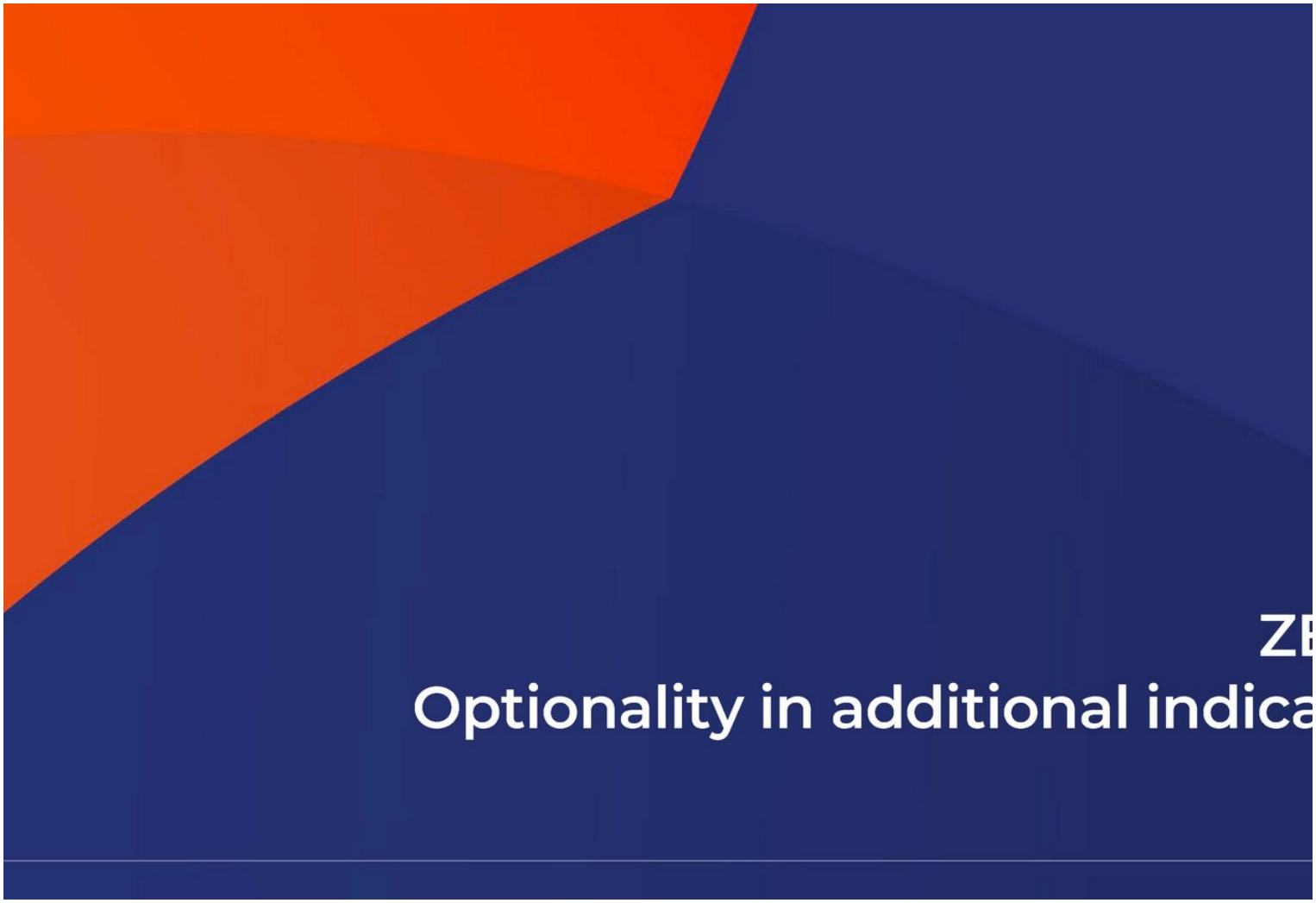

**Key efficacy endpoints:**

- HiSCR (50, 75, 100)
- Improvement in baseline AN counts
- IHS4
- PGA
- DLQI
- PK / PD assessments

**Key safety endpoints:**

- General Safety and Tolerability
- Severe infection
- Neutropenia

Note: Clinical development plans are subject to ongoing review, regulatory feedback


ZE
Optionality in additional indica

# Multiple External Readouts Continue to Validate Both IL-17 and BAFF Pathways in Additional Diseases

| | Unmet need | Evidence validating relevance of IL-17 and BAFF inhibition | Ext |
|---|---|---|---|
| **Sjögren's syndrome (SS)** | • It is estimated that there are **250,000 – 350,000 people living with Sjögren's in the U.S.**[1]<br>• Some estimates of the total global patient burden approach ~4M, with a smaller subset patients presenting most severely<br>• High unmet need as there are **no FDA-approved treatments for Sjögren's** | Multiple clinical readouts have validated the BAFF Pathway in Sjögren's including<br>• Novartis phase 2b data with BAFF-R lanalumab (VAY736)<br>• Remegen Telitacicept ph2 data<br>IL-17 pathway continues to be explored pre-clinically for Sjögren's Syndrome | • Ar ph<br>• Nc lar ph<br>• Re Tel rea |
| **Systemic Lupus Erythematosus (SLE)** | • Systemic lupus erythematosus (SLE) is the most common form of lupus, affecting approximately 70 percent of an estimated 5 million people with lupus worldwide[2]<br>• Approximately 170,000-200,000 Americans live with SLE. It is a chronic, incurable autoimmune disease producing autoantibodies that can attack almost any system in the body | tabalumab (BAFF) previous showed statistically significant efficacy in large 1,124 patient Ph3 study<br>Benlysta (BAFF) is approved in SLE and Lupus Nephritis (LN)<br>IL-17 pathway continues to be explored pre-clinically for SLE and LN | • Nc lar<br>• Re Tel |

Sources: Clinical Trials, Company Presentations and Wall Street Research
1. Maciel G, et al. Prevalence of Primary Sjögren's Syndrome in a US Population-Based Cohort. Arthritis care & research. 2017;69(10):1612-1616. 2. The Lupus Foundation of America

# Conclusion
# Investment Highlights

**Experienced and proven leadership**

- Experienced drug developers and asset hunters led by ex-Arena leaders
- Product approvals & commercialization
- Significant corporate transactions

**Multiple Phase 2 programs**

- Validated mechanisms pursuing innovative new development paths
- Potential Best in Class attributes combined with strategic clinical development to enhance differentiation

**Track Record of Execution**

- Deep relationships with KOL community
- Prior CRO leadership history within team enhances our Sponsor status
- Recent precedent of on-time execution in crowded I&I spaces (UC, AD, etc.) includes absorbing COVID impact without delays

**Strong and committed financial backing with long-term alignment**

- Investors aligned with long-term commitment
- Successful PIPE transformation, including $65M in funding through Business Combination

Abbreviations: AD, Atopic Dermatitis; CRO, Contract Research Organization; KOL, Key Opinion Leader; UC, Ulcerative colitis

Note: please see language in the Disclaimer regarding 'forward-looking statements'

# ZE
# A Potential Best-in-Class Anti
# Inhibiting Both IL7 and TSLP Path

Note: please see language in the Disclaimer regarding 'forward-looking statements'

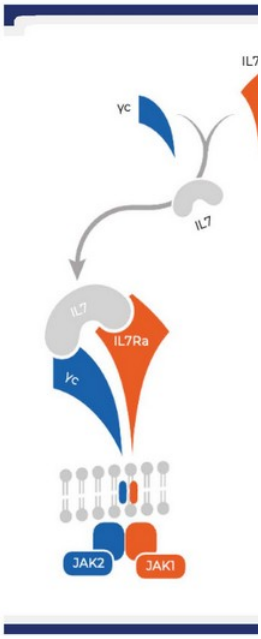
# ZB-168 – Asset Overview

### About ZB-168

- IL7Rα implicated in two key immune pathways[1]: IL7 and TSLP
- Only anti-IL7R program to date with human clinical data showing impact on key T-cell sub-populations[2]
- Well tolerated in >90 subjects and patients dosed in Phase 1 studies conducted by Pfizer[2,3]
- Utility in multiple T-cell driven diseases[4]

### Mechanism of Action

- Inhibition of IL7Rα blocks both IL7 and TSLP signaling[5]
- Blocking IL7Rα selectively inhibits survival/activity of effector memory and central memory CD4 and CD8 T cells while preserving the $T_{regs}$ compartment[1,5]
- T cell transcriptomics show downregulation of genes associated with activation, differentiation and trafficking of Th1, Th2 and Th17[6]
- Blocking TSLP reduces Asthma exacerbations in both Th2 high and low populations[7]




### Indication Areas of Potential Interest

- Respiratory
- Dermatologic
- Gastrointestinal

### Market Opportunity

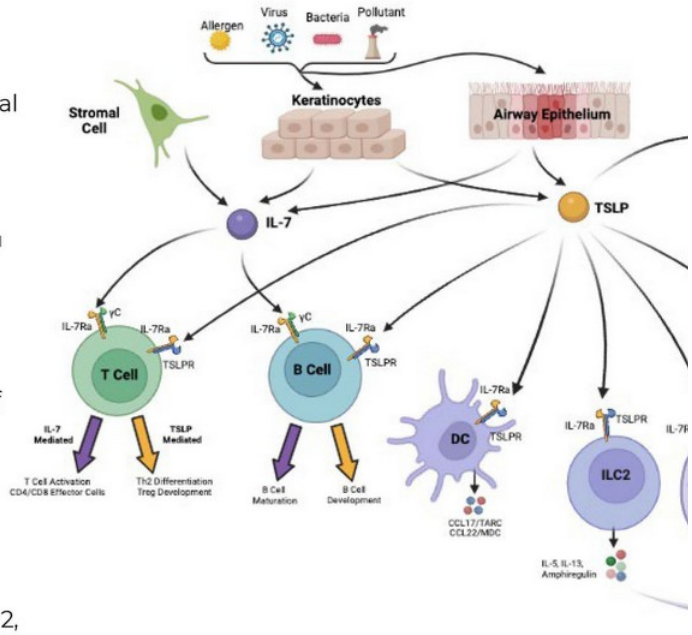
- Advances in the field further validate IL7 and TSLP in multiple type Th1 & Th2 immune disorders with significant global opportunities
- Potential 1st-in-class opportunities within several indications

1. doi: 10.1038/s41467-018-06804-y, 2. 10.1172/jci.insight.126054, 3. Clinical study report, 4. doi:10.3389/fimmu.2020.01557, 5. https://www.frontiersin.org/articles/10.3389/fimmu.2020.01557/full, 6. Herold,
4(23):e126054. 7. doi: 10.1056/NEJMoa2034975

# ZB-168 Enables Broad Impact on Epithelial-Driven Inflam by Targeting both TSLP and IL-7

## TSLP and IL-7 Pathways

- 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 exacerbating environmental factors and is an important amplifier of 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]
- 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 Treg:Teff ratio[5, 6]
- Dual inhibition of TSLP and IL-7 has potential to modulate Th1, Th2, and Th17-driven inflammation in a targeted manner across a broad number of allergic and autoimmune diseases[7]




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 In 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

# ZB-168 Has Broad Potential Therapeutic Applications

Inhibition of IL7R promotes a normalisation in $T_{reg}$ T-cell ratios[4]




Multiple Pote
Indications in
Therapeutic A

- Respirat
- Dermat
- Gastroin

TSLP is an early player in triggering airway inflam
the activation of several immune cells such as der
innate lymphoid cells, monocytes, macrophages a

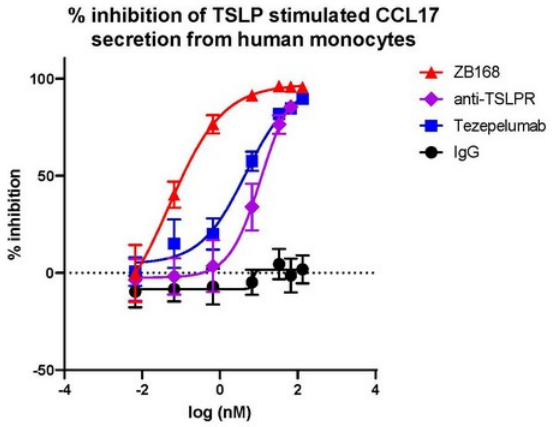
1. Eosinophilic esophagitis; 2. Chronic rhinosinusitis with nasal polyps; 3. Chronic spontaneous urticaria;
4. doi.org/10.3389/fimmu.2018.02692 & doi.org/10.1016/j.jsci.2020.101421 ; 5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6436879/

# ZB-168 is Potential Best-in-Class and Only Non-Partnered Asset in Development

| | ZB-168 | ADX-914 | OSE-127 | GSK2618960 | Tezepelumab | UP |
|---|---|---|---|---|---|---|
| Type of Antibody | **Human** | Human | Humanised | Humanised | Human | Hur |
| Target | **IL7Rα** | IL7Rα | IL7Rα | IL7Rα | TSLP | TSL |
| Mode of Administration | **SC**[2] | SC | IV[3] | IV | SC | IV |
| Lead Indications | **Alopecia Areata** | Atopic Dermatitis | Ulcerative Colitis; pSS[4] | Programme inactive | Asthma, CRSwNP | Ast |
| *Current Phase | **Phase 1b/2** | Phase 1b/2 | Phase 2 | Phase 1b | Approved | Pha |
| Humans Exposed | **HVs[5]: 60 subjects**<br>**Patients: 33 subjects** | HVs: ~32 subjects<br>Patients: asthma | HVs: ~63 subjects<br>Patients: Ulcerative colitis | HVs: 18 subjects<br>Patients: None | Patients: >1,000 | HVs<br>Pati |

*As of September 2022; 1. Thymic stromal lymphopoietin receptor; 2. Subcutaneous; 3. Intravenous; 4. Primary Sjögren's syndrome 5. Healthy volunteers

# ZB-168 is Potentially Best-in-Class Asset at TSLP Inhibitio




- ZB-168 is nearly **10-fold** more potent than AZ/AMG's tezepelumab, and tezepelumab does not inhibit IL7 signaling
- ZB-168 is >**300-fold** more potent than Q32Bio / Horizon's ADX-914 in TSLP-induced markers, but similar in IL7-induced pSTA5[4]

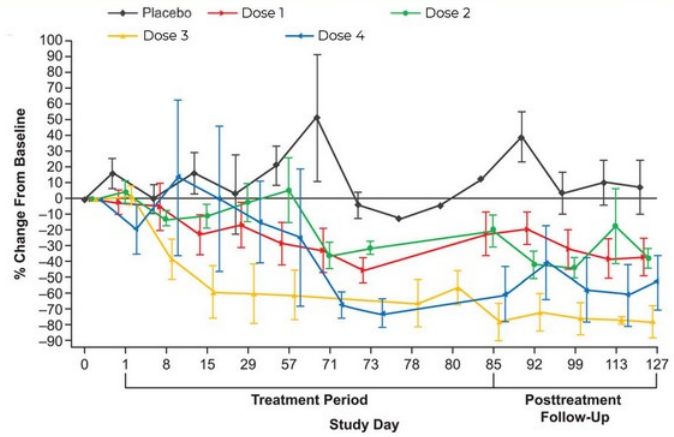
| | zurabio | UpstreamBio | AstraZeneca / AMGEN |
|---|---|---|---|
| **Asset** | **ZB-168 *(IL7Rα)*** | **UPB-101 (α-TSLPR)** | **Tezepelumab (TSLP)** |
| | IL7Rα mAb | α-TSLPR mAb | TSLP mAb |
| **TSLP-Induced Signals** | • 7.5 ng/ml / **0.05nM** (CCL17)[1]<br>• 11 ng/ml / **0.07nM** (CCL22)[1]<br>• **0.08 nM** (CCL2)[4] | • 16.1 ng/ml / **0.1nM** (CCL17)[3] | • 67 ng/ml / **0.44nM** (CCL17)[3] |
| **IL7-Induced Signals** | • 0.46nM (pSTAT5)[2] | Neg | Neg |

1. Zura Internal Data, 2. doi: 10.1172/jci.insight.126054, 3. doi: https://doi.org/10.1124/jpet.121.000686, 4. BMS patent https://patents.google.com/patent/WO2020154293A1/en

# ZB-168 is Further Differentiated by $T_{effector}$ Cell Inhibition

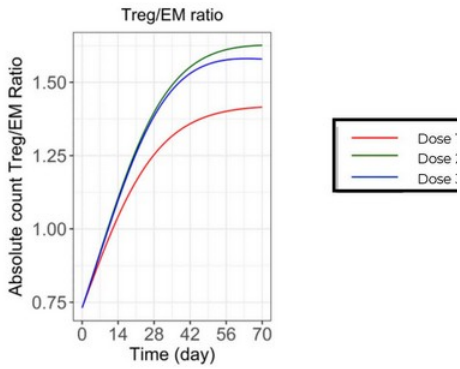
## Clinical data in patients demonstrates impact on key T-cell subpopulations

### CD8+ $T_{effector}$ cells[1]




- Up to 70% reduction in CD8+ $T_{effector}$ memory cells
- Similar reductions seen for naïve and central memory T-cells

### Ratio of $T_{reg}$ to $T_{effector}$ cells[2]




- Increases in ratios observed for all doses
- ZB-168 shows 20x greater potency for $T_e$ vs $T_{reg}$ cells

1. doi: 10.1172/jci.insight.126054, 2. doi:10.1208/s12248-019-0401-3

zurabio

# Summary of Clinical Data

- 93 subjects dosed with ZB-168 to date, including 33 patients with Type 1 Diabete Multiple Sclerosis[2]
- In Phase 1 single ascending dose study, ZB-168 was generally well tolerated with deaths and no subjects discontinued, or dose reduced due to Adverse Events (A
- Demonstrated significant clinically relevant biologic effects that may lead to a therapeutic benefit[1]
- Demonstrated proof of mechanism in a Phase 1b study of patients with recent o Type 1 Diabetes (activity in inducing tolerance)[1]

1. doi: 10.1172/jci.insight.126054, 2. Internal study report, 3. Internal study report

# torudoki
# Targeting Anti-IL33, an Alarmin
# Potential in Multiple Indica

# torudokimab – Asset Overview

### About torudokimab

- IL-33 implicated in driving Th2 biology through ST2 and Th1/Th17 through alternative signaling[1]
  - Drug well tolerated in Phase 1 and 2 trials conducted by Eli Lilly[2]:
    - 141 healthy volunteers in Phase 1 study
    - 103 patients with moderate to severe atopic dermatitis
    - Utility in diseases driven by epithelial inflammation

### Indication Areas of Potential Interest

- Respiratory
- Dermatologic
- Gastrointestinal
- Orphan autoimmune

### Mechanism of Action

- Inhibition of IL-33 blocks both ST2 and RAGE signaling[3]

### Market Opportunity

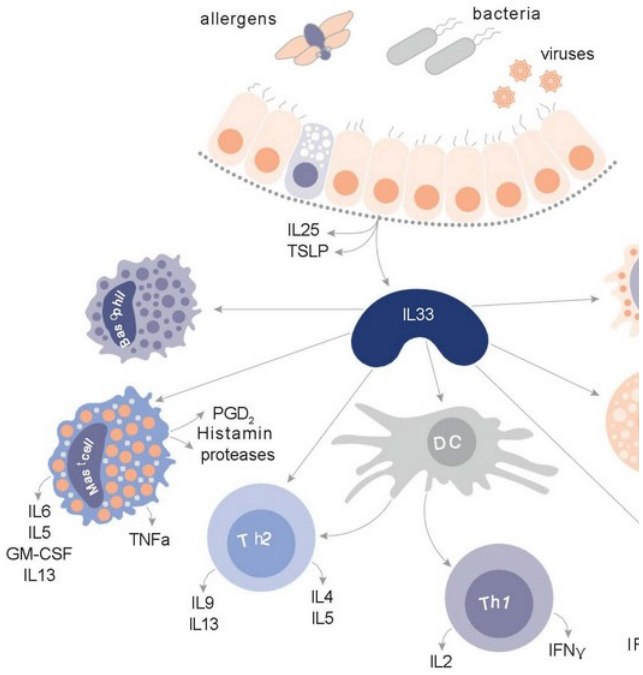
- Advances in the field further validate IL-33 in multiple respiratory disorders with significant global blockbuster opportunities
- Potential 1st and best-in-class opportunities within multiple indications
- Validated pathways in COPD4 and asthma[5]


1. Suzanne 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. Okragly et al Journal of Inflammation Research 2021:14 3823–3835, 4 . https://doi.org/10.1016/S2213-2600(22)00005-4, 5. doi:10.1056/NEJMoa2024257

# Targeting IL-33 In Epithelial Driven Diseases

## IL-33 Pathway

- IL-33 is a member of the IL1 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 IL33 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, COPD[3], 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]



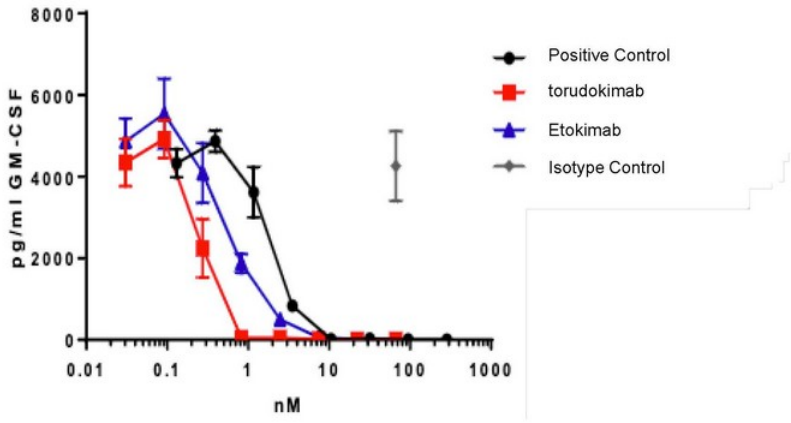

1. Chan, 2019. Frontiers Immunol, 2. doi.org/10.1016/j.cyto.2022.155891, 3. https://doi.org/10.1038/ng.323 and doi:10.1016/j.jaci.2020.04.051 , 4. :https://doi.org/10.1016/S2213-2600(22)00005-4; doi:10.1056/NEJMoa2024257 and doi: 10.1126/scitranslmed.aax2945 , 5. Sci Trans Med., Zura Bio Internal data,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

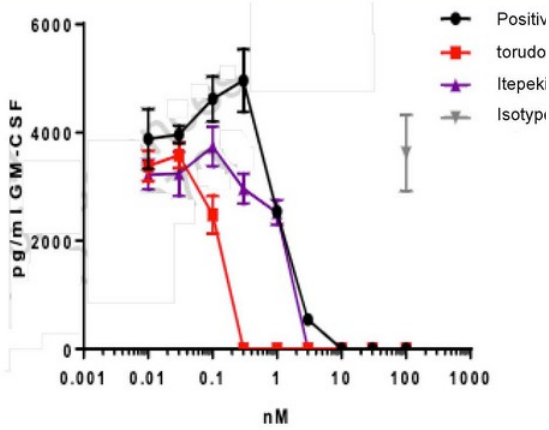


Note: please see language in the Disclaimer regarding 'forward-looking statements'

# 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 by human mast cells**




| Antibody | $k_{on}$ ($M^{-1}s^{-1}$) | $k_{off}$ ($s^{-1}$) | $k_d$ (pM) | Torudo |
|---|---|---|---|---|
| torudokimab (LY3375880) | $1.7x10^{6}$ | $6.7x10^{-5}$ | 39 | |
| etokimab (AnaptysBio) | $9.4x10^{5}$ | $1.2x10^{-4}$ | 112 | |
| itepekimab (Regeneron) | $7.6x10^{5}$ | $1.6x10^{-4}$ | 215 | |

Source: Zura Bio Internal data



Note: please see language in the Disclaimer regarding ‘forward-looking statements’

# Summary of Clinical Data

- >100 subjects dosed with torudokimab to date, including in a Phase 2 trial in atc dermatitis[1]
- In Phase 1 study, torudokimab was well tolerated and no safety concerns were identified in either the SAD or MAD portions
- The target engagement evaluation suggested binding to IL-33 and treatment emergent ADA had no apparent impact on PK or target engagement
- In Phase 2 study in atopic dermatitis, torudokimab was well tolerated and no sa concerns identified; despite overall non-significant efficacy, responder analyses confirms key biomarker reductions (IL13, periostin and CCL17/TARC) and no ADA impact[1]

1. doi.org/10.1111/bjd.21631

zurabio

Corporate Overview w
ZB-106 Deep-Dive

# Building the Next Immunology Leader

April 2023