ZL-1102
Proof-of-Concept Study
Topline Results

October 21, 2021

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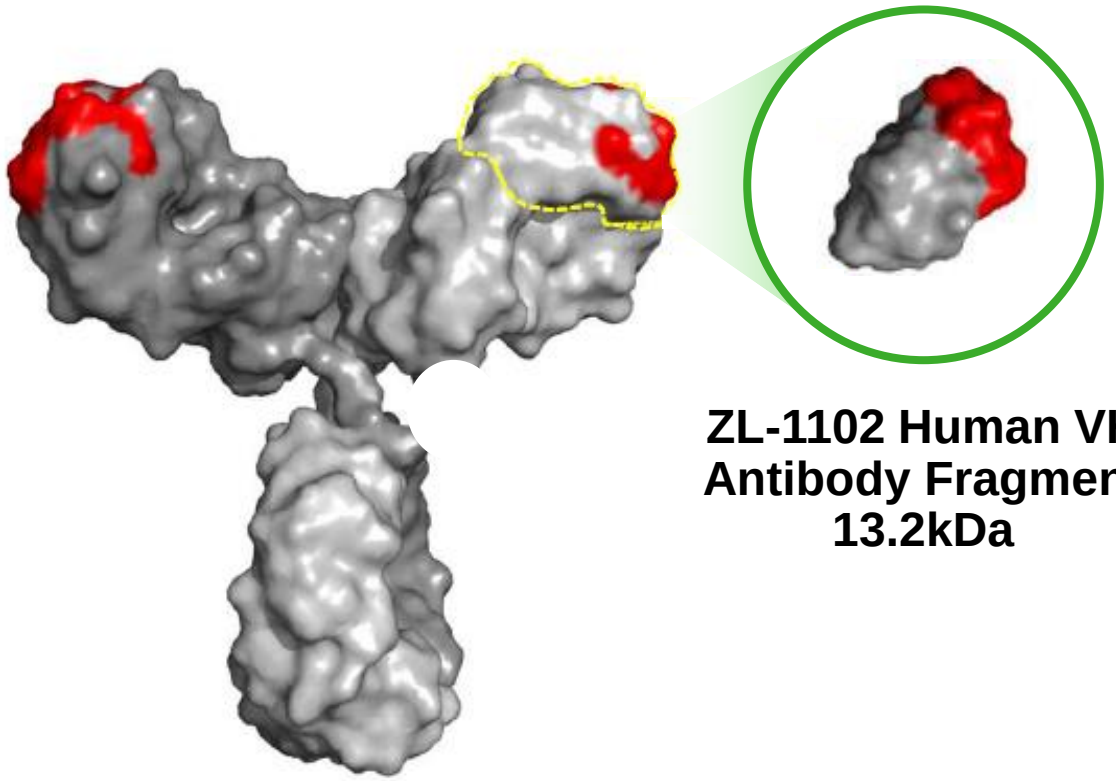
ZL-1102
High-Affinity Human VH Fragment Targeting IL-17A



ZL-1102 Human VH Antibody Fragment 13.2kDa

IgG Antibody 150 kDa

Topline Results from Proof-of-Concept Study

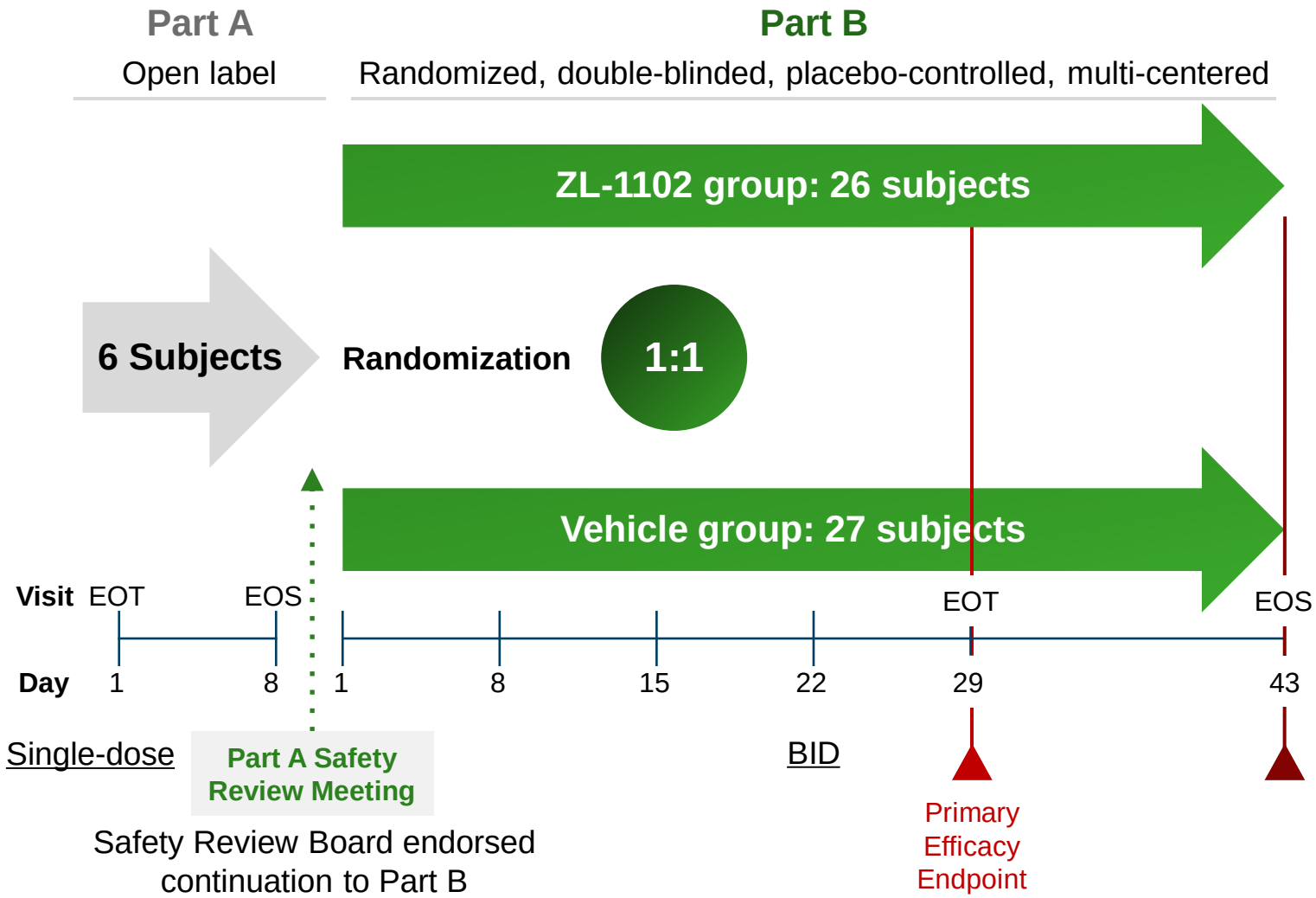
- Small anti-IL-17 Humabody®, or human VH antibody fragment, for **topical** treatment of **mild-to-moderate** chronic plaque psoriasis (CPP)
- Topical therapy with ZL-1102 resulted in approximately a 45% relative improvement in local PASI score, improvement in erythema and scaling, reduction in target lesion size, and improved responder rates compared to placebo in patients with mild-to-moderate CPP
- Consistent clinical improvement was seen over time
- First-ever study to demonstrate **penetration of protein biological** through psoriatic skin resulting in clinical response
- Safety profile comparable to placebo

Note: Humabody is a registered trademark of Crescendo Biologics.

ZL-1102 Protocol Overview – Study Design

Entry Criteria

1. Mild / moderate CPP
2. At screening and baseline:
   a. PASI ≤15; affected BSA ≤10%
3. Suitable psoriatic plaque (ALL criteria apply):
   a. Lesion size: 9-100 cm^2
   b. Lesion stable for ≥3 months
   c. Lesional PASI score ≥8



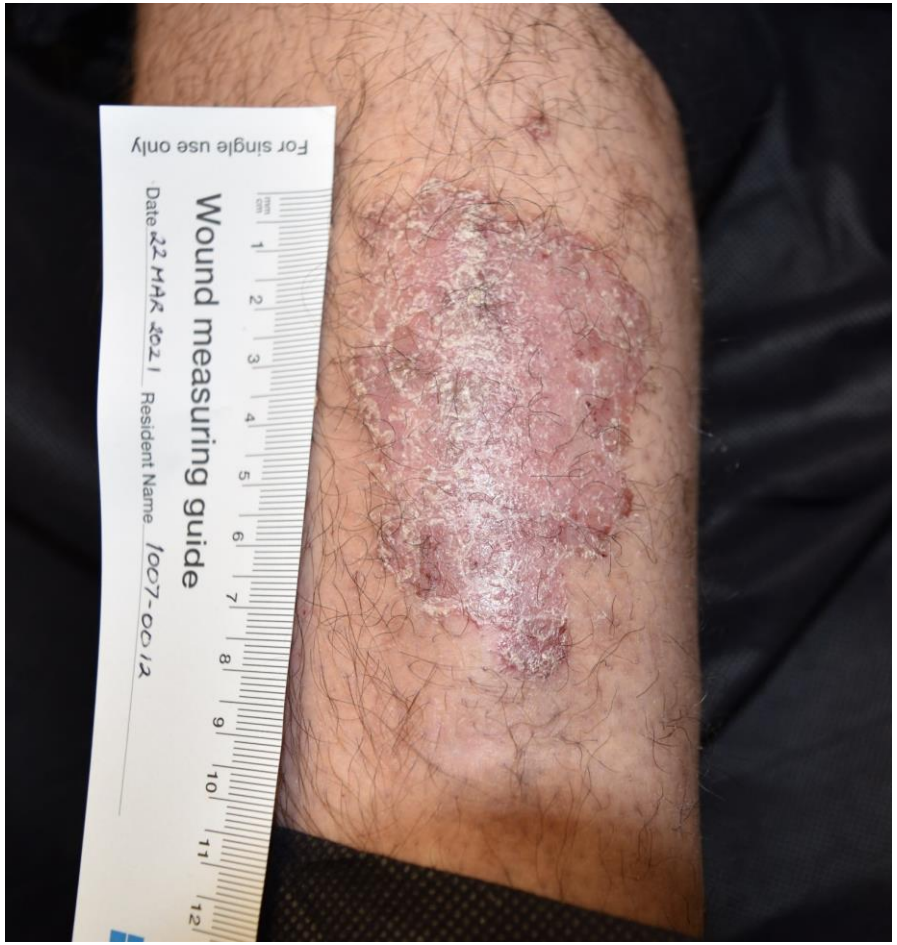
Note: End of treatment (EOT), end of study (EOS).

Proof-of-Concept Phase 1b Study – Overview and Results

Goals	Efficacy in CPP by trend, safety/tolerability, PK, evidence of penetration
	Basis for Go/No Go decision
Clinical Results	Approx. 45% in relative improvement compared to placebo in local PASI[1] score of the target lesion at 4 weeks (primary efficacy endpoint)
	Consistent improvement in local PASI components over time: erythema > scaling > induration
	Consistent improvement in target lesion size (reduction in area) compared to an area increase in the placebo arm
	Consistently higher responder rates[2] over time compared to placebo
	Benign safety and tolerability profile comparable to placebo, with treatment-emergent adverse events (TEAEs) that were few in number and mild
PK	No systemic absorption by PK
Histology	Reduction in epithelial thickness on histology
Biomarkers	Full results pending

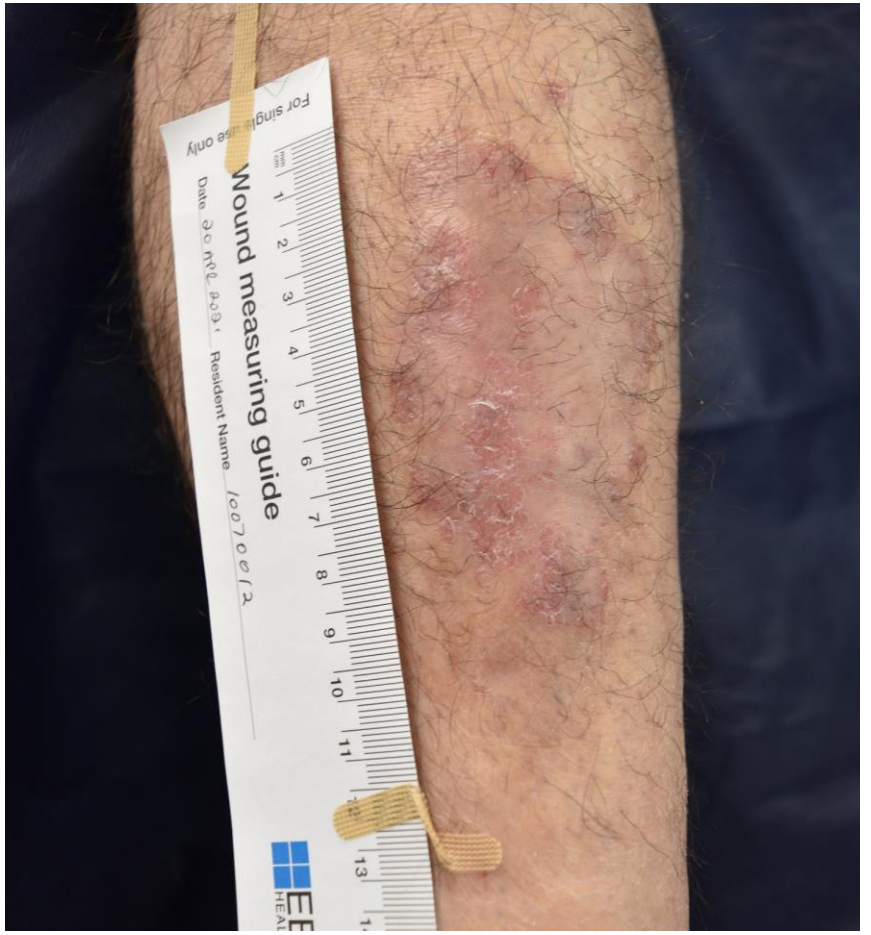
Note: (1) PASI = Psoriasis Area Severity Index; (2) The responder rate in this study was defined as the percentage of patients who achieved a ≥50% reduction compared to baseline in local PASI score of the target lesion, measured weekly.

Improvement in Local PASI Score – Case A



D1

Local PASI=8

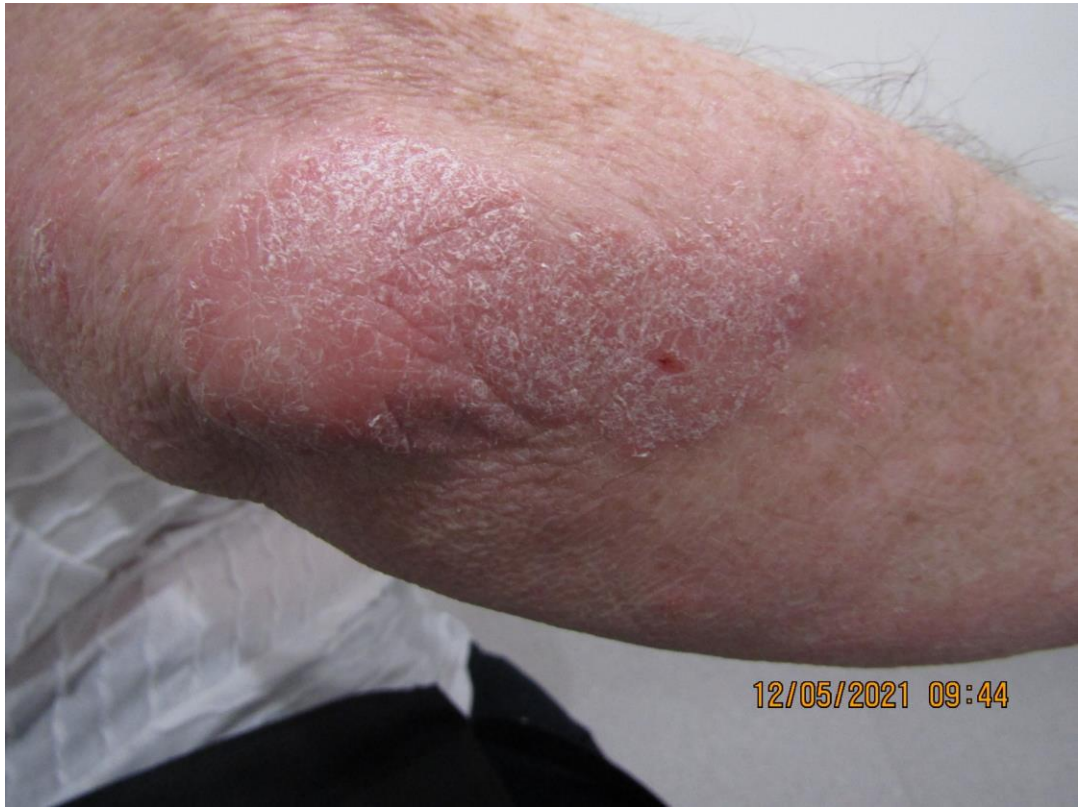


D29

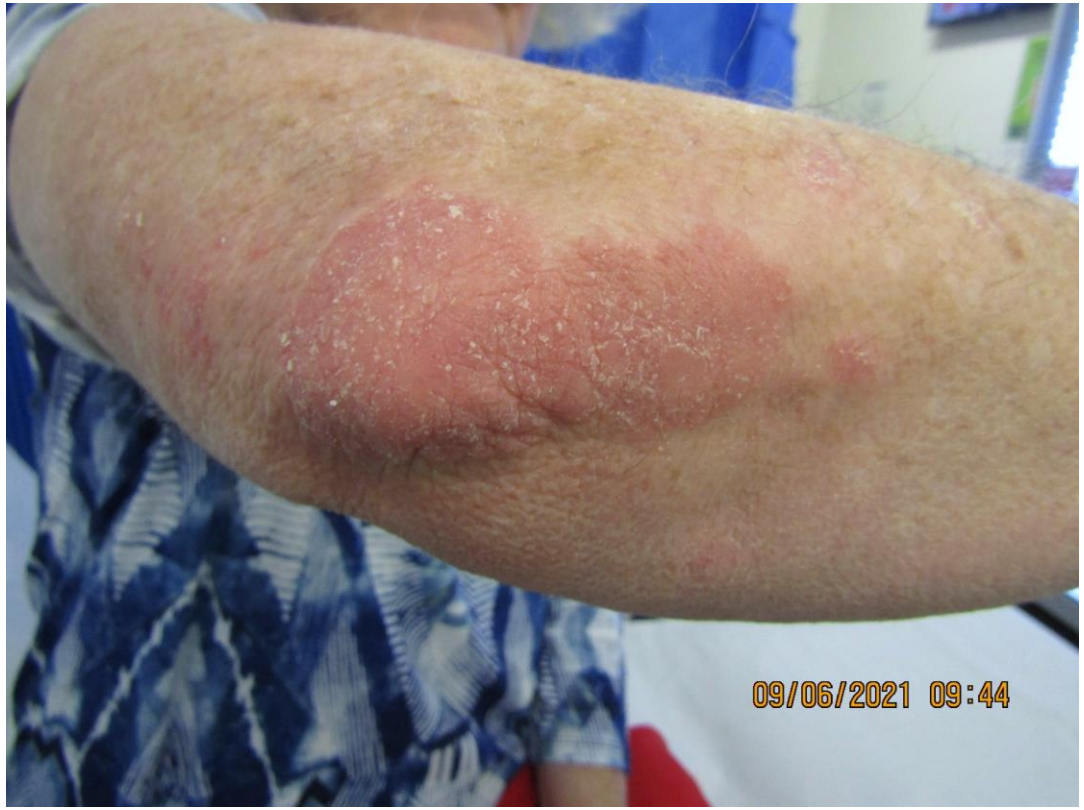
Local PASI=4

Note: PASI = Psoriasis Area Severity Index.

Improvement in Local PASI Score – Case B



D1
Local PASI=8



D29
Local PASI=4

Note: PASI = Psoriasis Area Severity Index.

Marketed IL-17 Inhibitors Are SC or IV
Do Not Target Mild-to-Moderate Psoriasis

- Role of **IL-17** confirmed in clinical studies in **moderate-to-severe CPP**[1]
- IL-17 antibodies associated with **systemic immunosuppression**, limited to more severe patient population[2]
- **No IL-17 mAbs approved for mild-to-moderate CPP**

Approved Agents in Psoriasis

MOA	Agent	Formulation	Marketed Indications
IL-17A	ixekizumab TALTZ	SC	Ankylosing spondylitis; Erythrodermic psoriasis; Plaque psoriasis; Psoriatic arthritis; Pustular psoriasis
	secukinumab COSENTYX	SC/IV	Ankylosing spondylitis; Plaque psoriasis; Psoriatic arthritis; Pustular psoriasis
IL-17A/F	bimekizumab BIMZELX	SC	Plaque psoriasis
IL-17RA	brodalumab SILIQ	SC	Erythrodermic psoriasis; Plaque psoriasis; Psoriatic arthritis; Pustular psoriasis

Strong rationale and patient need to develop a topical formulation of an IL-17-directed therapy that works directly on the lesion and avoids systemic exposure

Source: (1) Alan Menter et al, Interleukin-17 and Interleukin-23: A Narrative Review of Mechanisms of Action in Psoriasis and Associated Comorbidities, Dermatol Ther, 2021; (2) N D Loft et al, Adverse events with IL-17 and IL-23 inhibitors for psoriasis and psoriatic arthritis: a systematic review and meta-analysis of phase III studies, *J Eur Acad Dermatol Venereol*, 2020.

Summary

Significant Market Opportunity for ZL-1102

- Psoriasis affects approximately **125 million**[1] people worldwide; plaque psoriasis is the most common type, affecting 80 to 90% of those with psoriasis[1,2]
- **70–80%**[3] of plaque psoriasis cases are mild-to-moderate, and marketed IL-17 inhibitors are **currently not indicated** for such cases
- Topical therapies are the standard of care for treatment of mild-to-moderate disease. However, current treatment options **provide limited efficacy** or **have safety concerns with long-term use**
- This is the **first study** to demonstrate **penetration of a protein biological** through psoriatic skin resulting in a clinical response

Next Steps

- Zai Lab plans to advance compound into full development, including registrational studies
- Zai Lab plans to present the complete data at an upcoming scientific meeting and to submit them for publication

Source: (1) National Psoriasis Foundation. The impact of psoriasis. Available from: https://www.psoriasis.org/psoriasis-statistics/; (2) Menter A, Gottlieb A, et al. “Guidelines of care for the management of psoriasis and psoriatic arthritis, Section 1: Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics.” J Am Acad Dermatol. 2008; 58:826-50.; (3) Kim A Papp, et al. Psoriasis Prevalence and Severity by Expert Elicitation. Dermatol Ther 2021.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