

Phase 2b Trial of Zabalafin Hydrogel, A Novel Topical Botanical Drug That Addresses The Four Demons of Atopic Dermatitis

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Learning Objectives

Understanding the AD Disease Continuum is 4 distinct interconnected problems, the “4 Demons” of AD, that are the Inflammation Component, the Bacterial Component, Pruritus and Xerosis, which must be treated and managed.

Understanding Zabalafin Hydrogel is a promising new topical botanical drug for managing AD across all ages, based on Phase 2a clinical trial results presented here and emerging Phase 2b clinical trial trends.

Take Away Messages

The AD Disease Continuum must be treated and managed.

Recognize the potential of Zabalafin Hydrogel to directly target the entire AD Disease Continuum for the sustained treatment and management of AD, because Zabalafin Hydrogel has multi-mechanisms of action.

Conflict of Interest: This research was funded by Alphyn Biologics, Inc.
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Schachner et al Reports An Effective Therapeutic Directly Treats All “4 Demons” of Atopic Dermatitis ¹

The “4 Demons” of AD

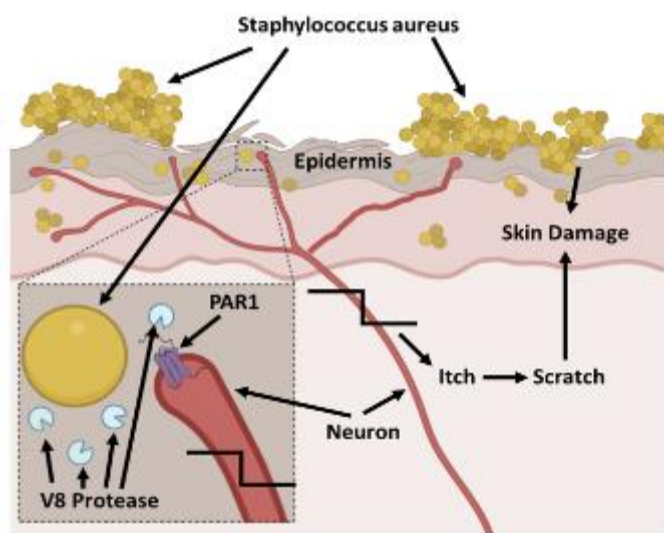


- Current drugs primarily treat directly only 1 of the “4 Demons” of Atopic Dermatitis: the Inflammation Component
- The ideal AD drug should treat all “4 Demons” of Atopic Dermatitis

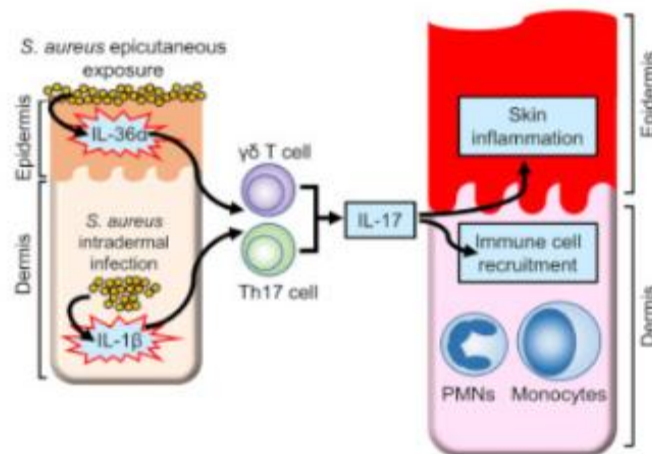
¹ [The Atopic Dermatitis Continuum: An Updated Paradigm for a Common Disorder and a Novel Multipurpose Treatment Option - JDDonline - Journal of Drugs in Dermatology](#), Option Schachner et al, JDD, Sept. 2025, Vol 24

Bacteria - *Staph* - Makes Atopic Dermatitis Worse ^{1, 2, 3, 4}

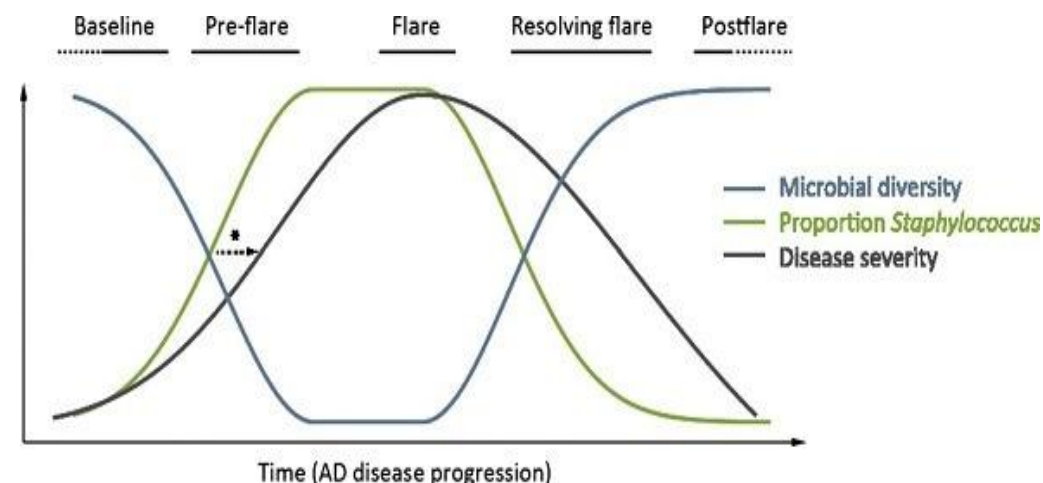
Deng et al Demonstrate Bacteria Causes Itch ²



Liu et al Demonstrate Bacteria Causes Inflammation ³



NIH Demonstrate Staph Causes Bacteria Dysbiosis and AD Disease ⁴



¹ MRSA correlated to eczema? An interview with Dr Bjorn Herpers, News, Medical Life Sciences August 31, 2016, www.news-medical.net/news/20160831/MRSA-correlated-to-eczema-An-interview-with-Dr-Bjorn-Herpers.aspx

² *S. aureus* drives itch and scratch-induced skin damage through a V8 protease-PAR1 axis, liwen Deng,1 Flavia Costa,2,10 Kimbria J. Blake,1,10 et al Isaac M. Chiu,1,11, <https://doi.org/10.1016/j.cell.2023.10.019>

³ *Staphylococcus aureus* Epidermal Exposure Drives Skin Inflammation via IL-36-Mediated T Cell Responses, Liu, H., et al. (2017). Cell, Volume 22, Issue 5p653-666.e5, November 08, 2017, <https://pubmed.ncbi.nlm.nih.gov/29120743/>

⁴ Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis, Kong, HH et al, Genome Research. 2012 May; 22(5): 850–859. doi: 10.1101/gr.131029.111. www.ncbi.nlm.nih.gov/pmc/articles/PMC3337431/

Targeting the “4 Demons”

The Atopic Dermatitis Continuum: An Updated Paradigm for a Common Disorder and a Novel Multipurpose Treatment Option

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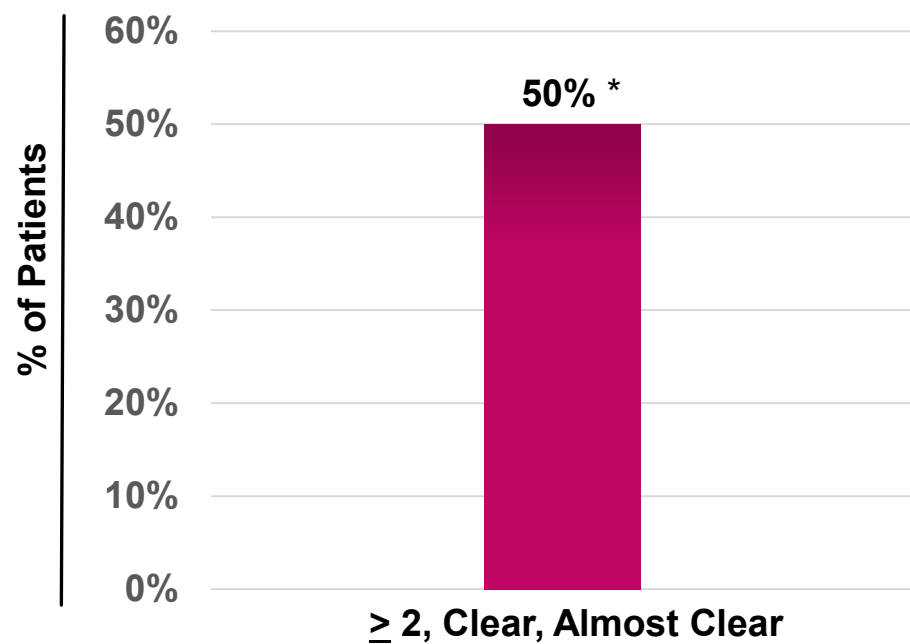
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- The AD Disease Continuum is 4 distinct interconnected problems, perpetuating and exacerbating one another, that must be treated and managed
- The 4 AD disease continuum problems are called the “4 Demons” of AD
 1. The inflammation component
 2. The two-fold bacterial component
 - Change in the normal bacteria on the skin (AD Bacterial Colonization Stage)
 - Bacteria on the skin that has progressed to AD Bacterial Infection Stage
 3. Itch
 4. Dry skin
- Effectively treating the AD Disease Continuum is complicated but must be achieved for effective disease management
- The AD Disease Continuum is not effectively served by current drugs because they directly target only one of these four AD problems, inflammation
- Effectively treating the AD Disease Continuum requires a direct, multi-target approach
- Zabalafin Hydrogel directly targets the entire AD Disease Continuum for the sustained treatment and management of AD
- Zabalafin Hydrogel AD Phase 2a Clinical Trials - Completed
 - “A randomized, double-blind, vehicle-controlled 4-week trial evaluated the safety and efficacy of zabalafin hydrogel for treating AD in individuals ages 2 and older”
- Zabalafin Hydrogel AD Phase 2b Clinical Trials – Currently enrolling

Phase 2a: Zabalafin Effective in Treating AD's Inflammation Component

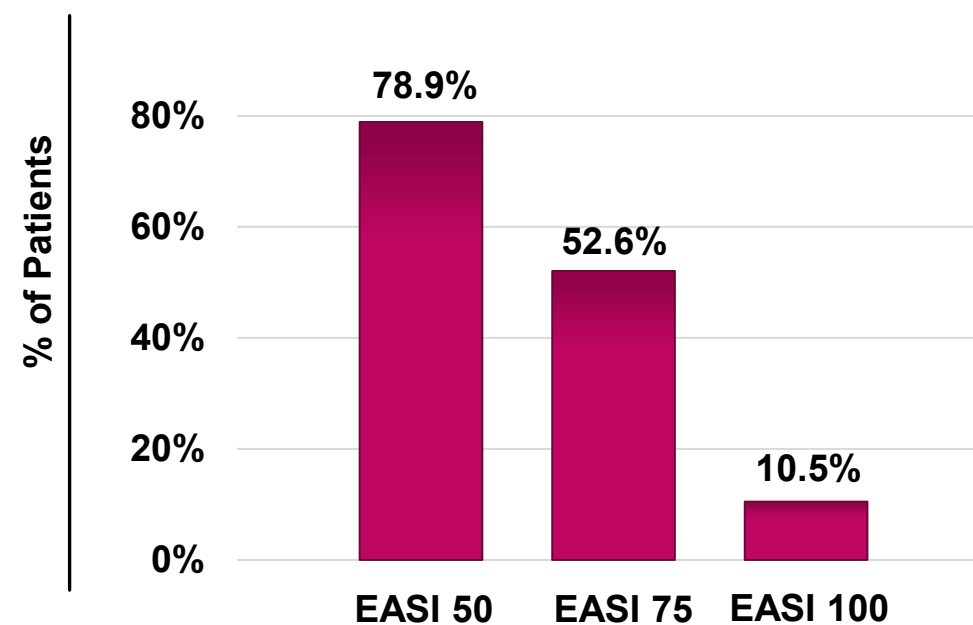
Zabalafin IGA



Zabalafin Hydrogel

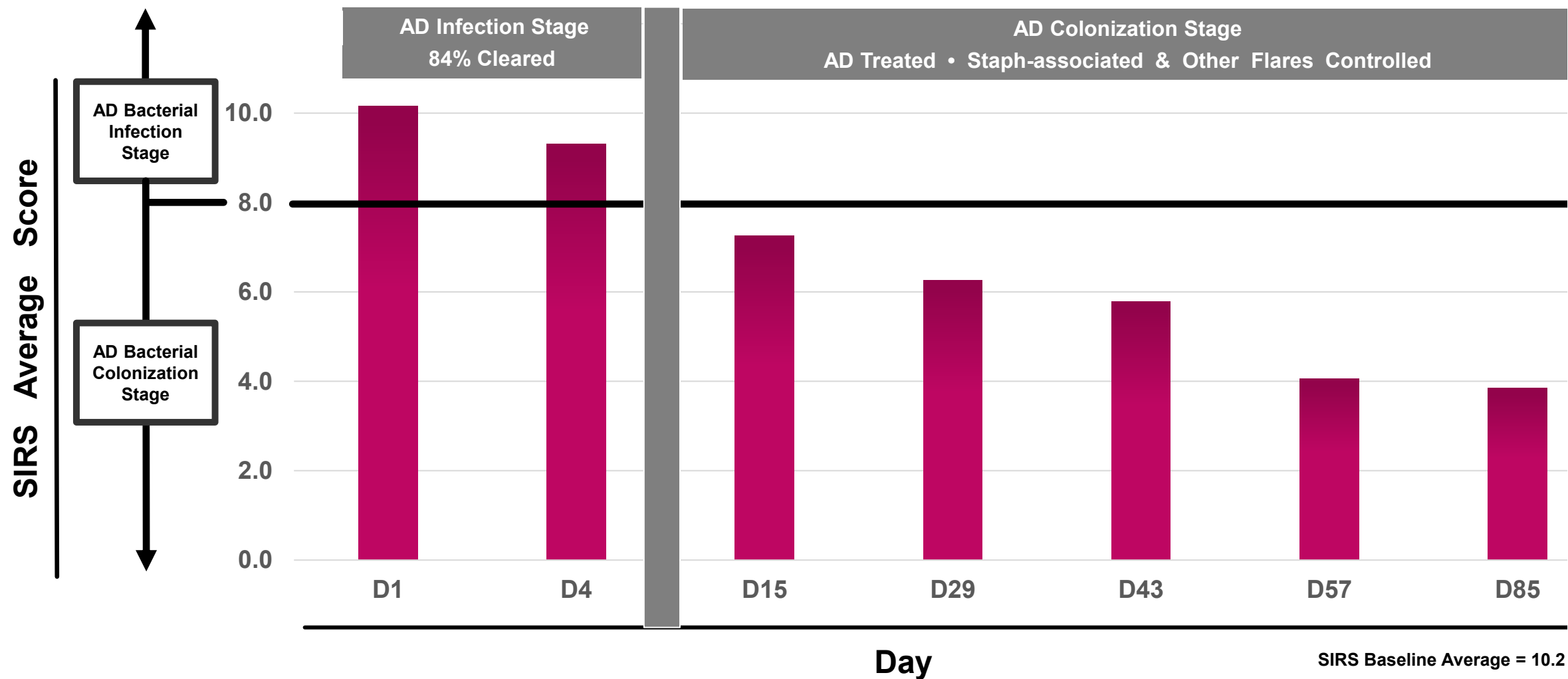
* 12 Weeks

Zabalafin EASI



Zabalafin Hydrogel

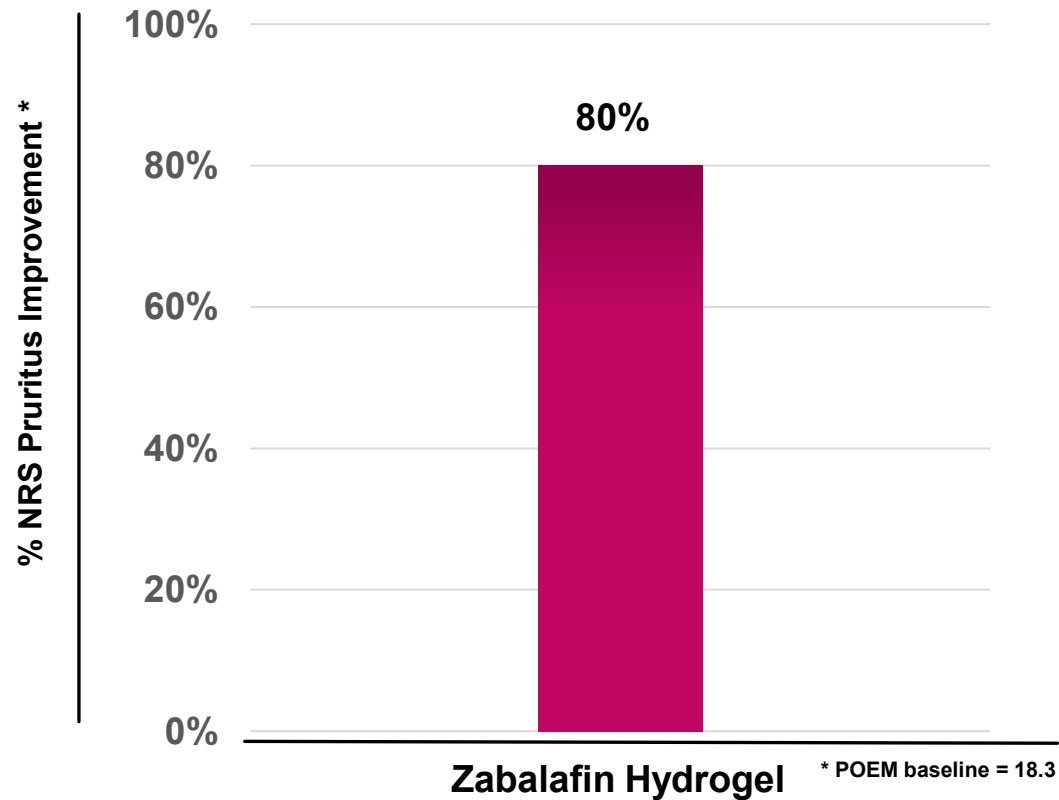
Phase 2a: Zabalafin Effective in Treating AD's Bacterial Component



Phase 2a: Zabalafin Effective in Treating Itch in AD

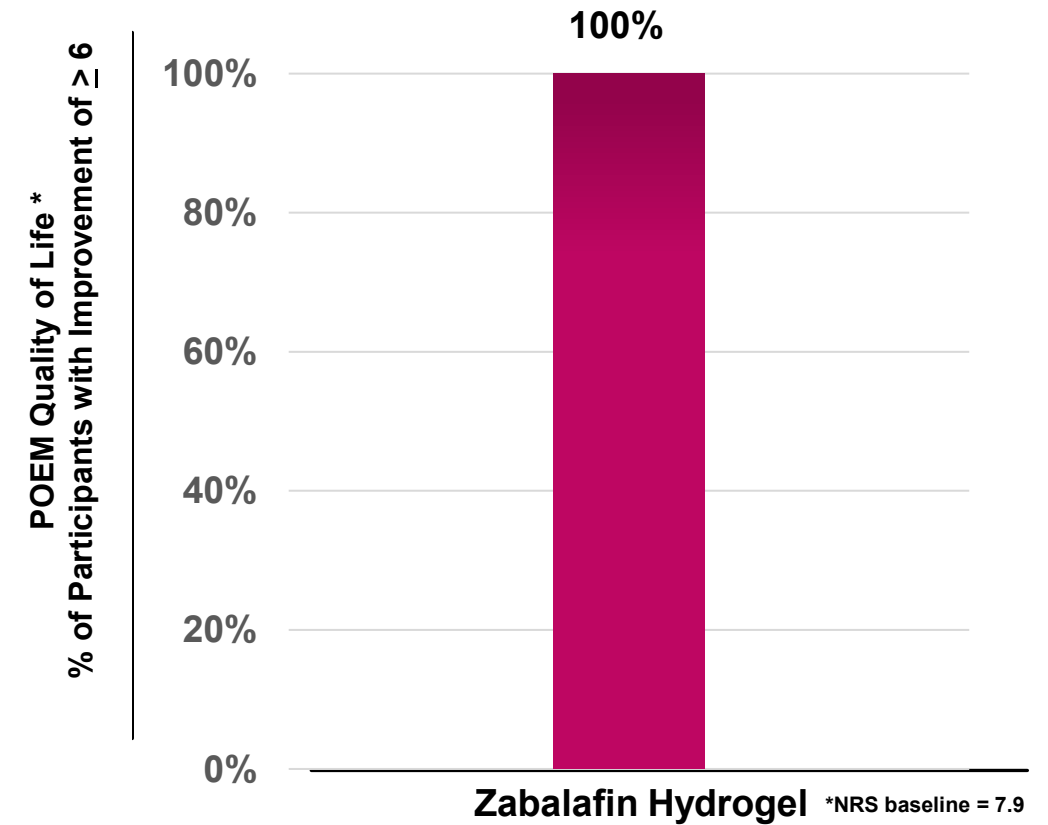
80% Achieved NRS Improvement of ≥ 4 at 8 weeks

Primary reason AD sufferers visit the doctor



Strong Improvement in Quality of Life

Primary reason AD sufferers visit the doctor



Zabalafin Ongoing Phase 2b Clinical Trial

If the data trends hold on unblinding, these results point to better results than seen in the Phase 2a program

- 16 week
- Double-blind
- Vehicle controlled
- Randomized 2:1
- All standard AD endpoints
- **Plus – Endpoints unique to Zabalafin treating bacteria cause of AD**
- All Mild and Moderate AD
 - AD Disease **Bacterial Colonization Stage**
 - AD Disease **Bacterial Infection Stage (unique to this drug)**