Efficacy and Safety of SD-101 Cream in Patients with Epidermolysis Bullosa: Results From a Phase 2b Study

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DISCLOSURE OF RELATIONSHIPS WITH INDUSTRY

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F097 – Late-breaking Research

DISCLOSURE

Investigator and consultant for Scioderm/ Amicus

Epidermolysis Bullosa (EB)

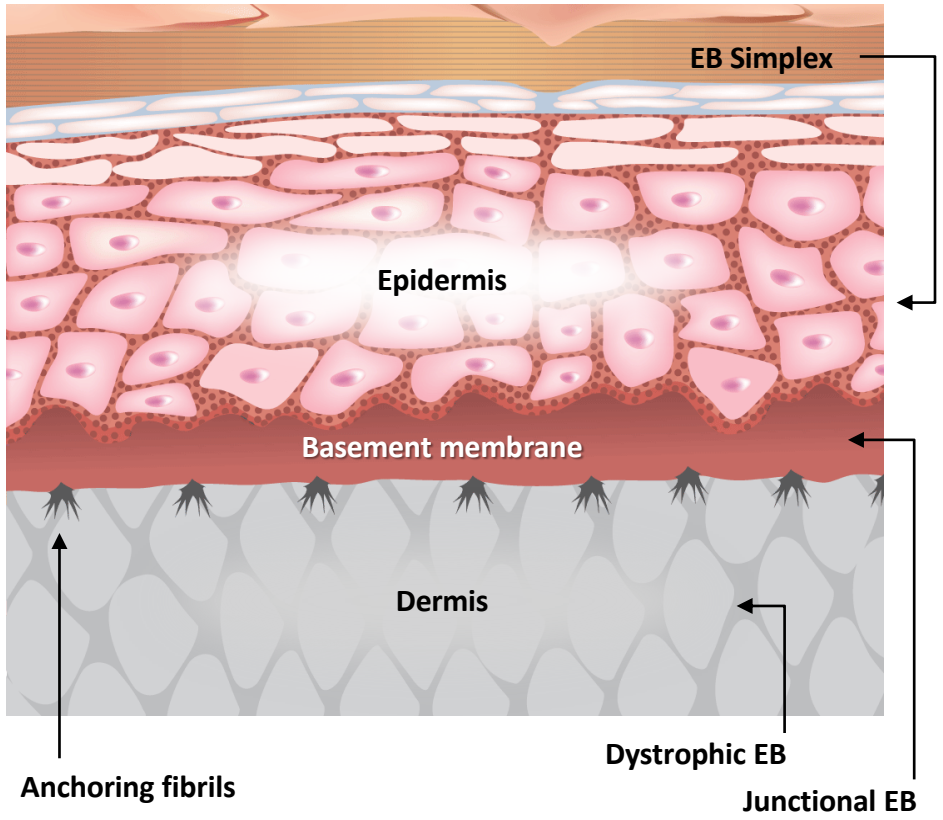
Hereditary Blistering Disorders without Approved Treatments

- Mutations in several genes cause EB, leading to fragility of skin and mucosal surfaces
- Usually diagnosed in neonates
- Severe blistering, open wounds in response to minor friction to the skin
- Residual scarring in forms with deeper blisters
- Disfiguring, excruciatingly painful, and can be fatal
- Given few treatment options, any reduction in disease signs and symptoms would be considered meaningful
- 30,000 – 40,000 diagnosed patients in major global regions

Differ By Physical Manifestations, Genetic Makeup, and Prognosis

Skin structure

Sites of primary blister formation



EB Types

Represent ~99% of EB Population

Subtypes	Symptoms	Frequency	Mortality risk
Junctional	▪ Blistering of skin/ mucosae ▪ Severe complications, esp. infection ▪ Usually fatal early in life	**~5%**	
Dystrophic	▪ Skin and mucosal blistering ▪ Scarring leads to narrowing of esophagus and orificial constriction ▪ Growth retardation, anemia ▪ Higher risk of aggressive skin cancer, esp after 1st decade	**~20%**	
Simplex	▪ Superficial blistering with variable extent and mucosal involvement	**~75%**	

Source: Adapted from DebRA America

SD-101 Overview

Patented High Concentration Allantoin with Breakthrough Therapy Designation

Active Ingredient & ROA	Proprietary topical cream containing 6% allantoin, applied to entire body once daily
Proposed Indication	All major EB types (Simplex, Dystrophic, Junctional)
Development Phase	Phase 3 registration study (SD-005) ongoing
Proposed MOA*	Aids inflammatory response, bactericidal effects, loosens protein bridges, promotes collagen
Formulation	Patented formulation to deliver high concentration in highly stable, soluble form

*Margraf and Covey 1977; Meixell and Mecca 1966; Settle 1969; Flesch 1958; Fisher 1981; Cajkovac et al., 1992; Medda 1976

3-Month Double-Blind Treatment Period[1]

48 EB patients (age ≥ 6 months)[1] - 1:1:1 Randomization - Daily Topical Application

SD-101 6% (n=15)

SD-101 3% (n=16)

Placebo (n=17)

Optional Extension (SD-004)

Open-Label SD-101 6%

42/44 Patients entered extension study

$400K FDA Grant for Extension Study

Primary Efficacy Endpoint: Target Wound Healing at Month 1

- Baseline wound: Chronic (≥ 21 days), size 5-50 cm^2

Secondary Efficacy Endpoints Include:

- Time to target wound closure
- Change in Body Surface Area (BSA) of lesional skin

[1]Assessments: 0, 14, 30, 60, 90 Days
[2]Initial Disease Severity: Mean target lesion size (cm^2)
14.0 (range 5-39)
Mean lesional BSA: 19.4% (range 0.4-48%)
Mean wound age (days): 182 (range 21-1,639)

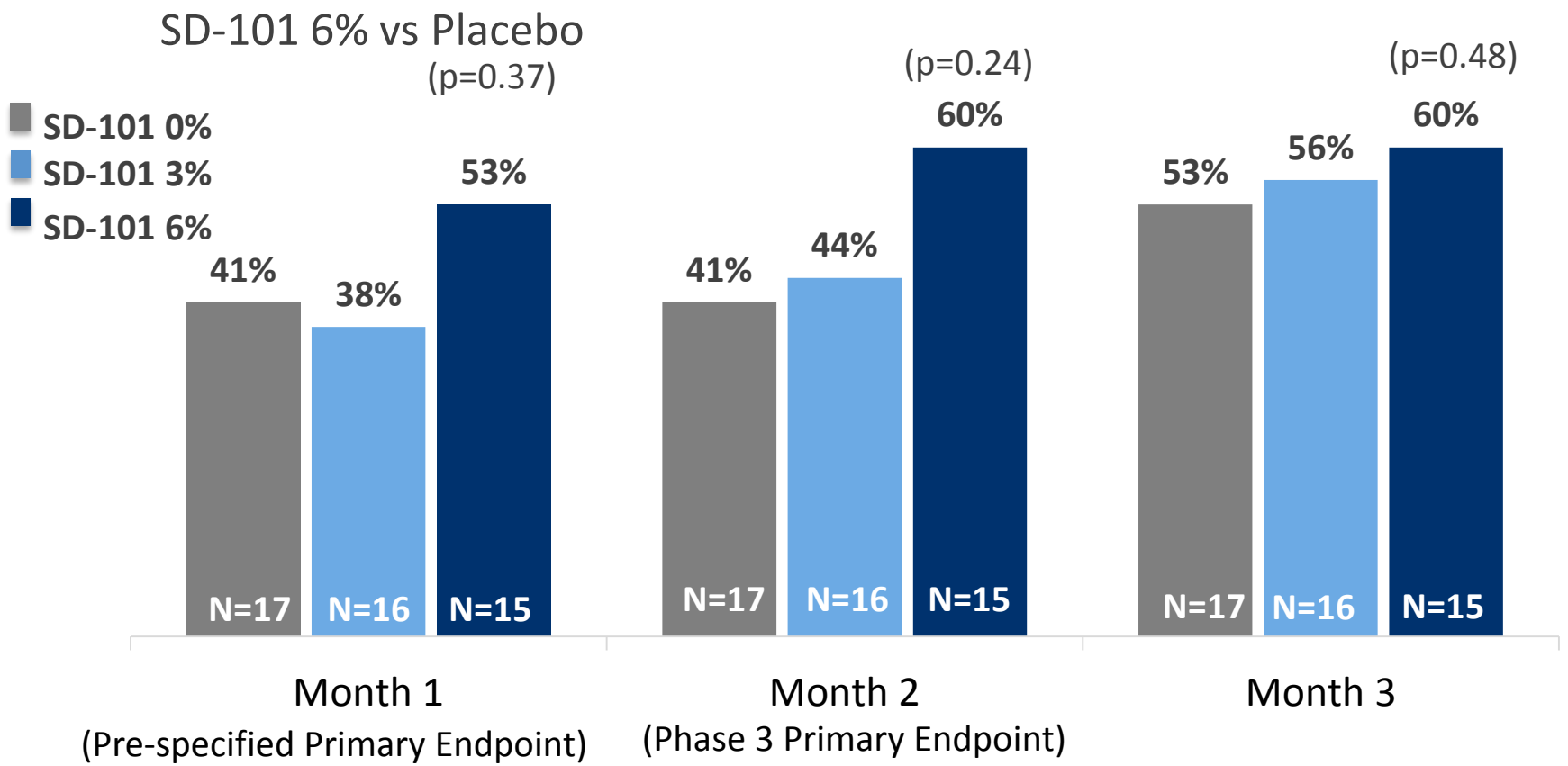
Study 003

- Demographics
  - Study population age: 6 months to 43.6 years with a mean age of 12.2 years
  - Majority of the ITT population was White/Caucasian (87.5%)
  - Balance of male and female patients
- Median (range) baseline target wound size
  - 9.5 cm^2 (5.2, 39.4) in the SD-101-0.0 group
  - 9.2 cm^2 (5.0, 34.7) in the SD-101.3.0 group
  - 7.6 cm^2 (5.0, 32.7) in the SD-101-6.0 group
- Disease subtype of patient population
  - 11 patients with EB Simplex (3 or 4 in each group)
  - 29 patients with Recessive Dystrophic EB (9 or 10 in each group)
  - 8 patients diagnosed with Junctional EB (2 or 3 in each group)
  - Subtypes evenly balanced across treatment arms

SD-101 6% Trended towards Higher Proportion of Complete Target Wound Closure

ITT Population (n=48)

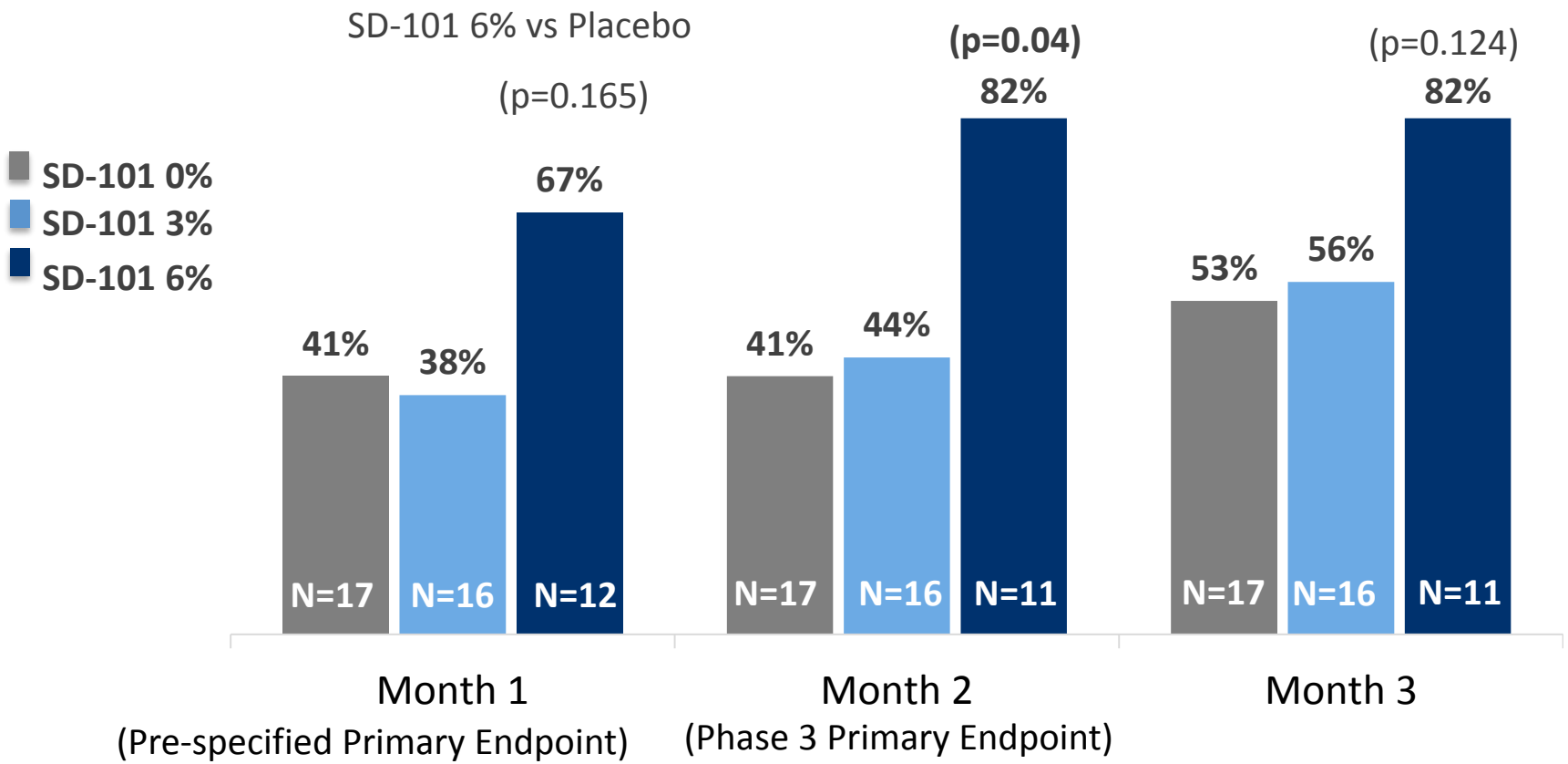
Proportion of Complete Target Wound Closure (%)



SD-101 6% Demonstrated Higher Proportion of Complete Target Wound Closure

Evaluable Population[1] (n=45)

Proportion of Complete Target Wound Closure (%)

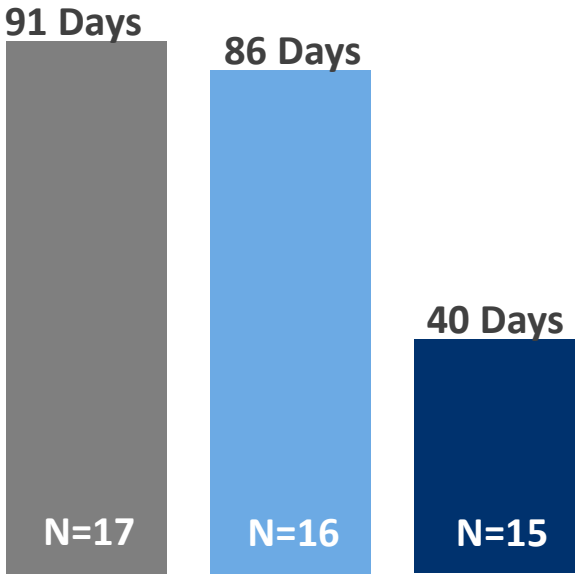


1. Excluded from Evaluable population: 1 patient (due to lost to follow-up), 2 patients (did not have single identified and qualified target lesion). 1 additional patient lost to follow up after Month 1 visit and is excluded from target wound assessment at later time points

SD-101 6% Showed Fastest Time to Target Wound Closure

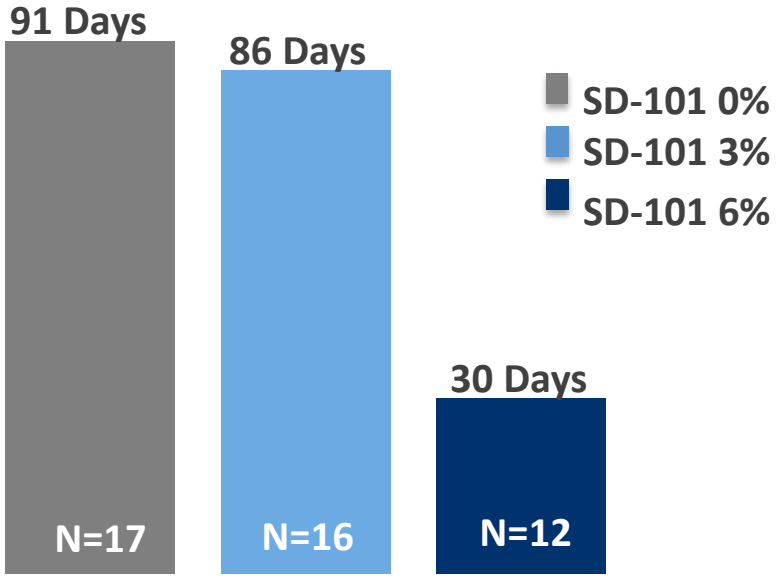
ITT Population (n=48)

Median Time to Target Wound Closure (Days)



Evaluable Population (n=45)

Median Time to Target Wound Closure (Days)



Adverse Events Similar Across Placebo, SD-101 3%, and SD-101 6%

- Treatment-emergent adverse events (TEAE) generally similar across treatment groups
- No deaths and no severe TEAEs
- No serious adverse events reported in SD-101 6% group

Treatment Emergent Adverse Events ≥10% Frequency

	SD-101 0% (Placebo)	SD-101 3%	SD-101 6%
N subjects	17	16	15
N subjects with TEAEs (%)	12 (70.6)	13 (81.3)	9 (60.0)
Nasopharyngitis	12%	25%	7%
Pyrexia	12%	19%	33%
Application Site Pain	6%	19%	13%
Pain	-	-	13%
Pruritus	6%	13%	13%
Rash	12%	-	7%
Rash Erythematous	12%	-	-
Cough	6%	-	13%
Oropharyngeal Pain	12%	-	-
Rhinorrhea	-	-	13%
Vomiting	6%	6%	13%
Headache	12%	-	7%

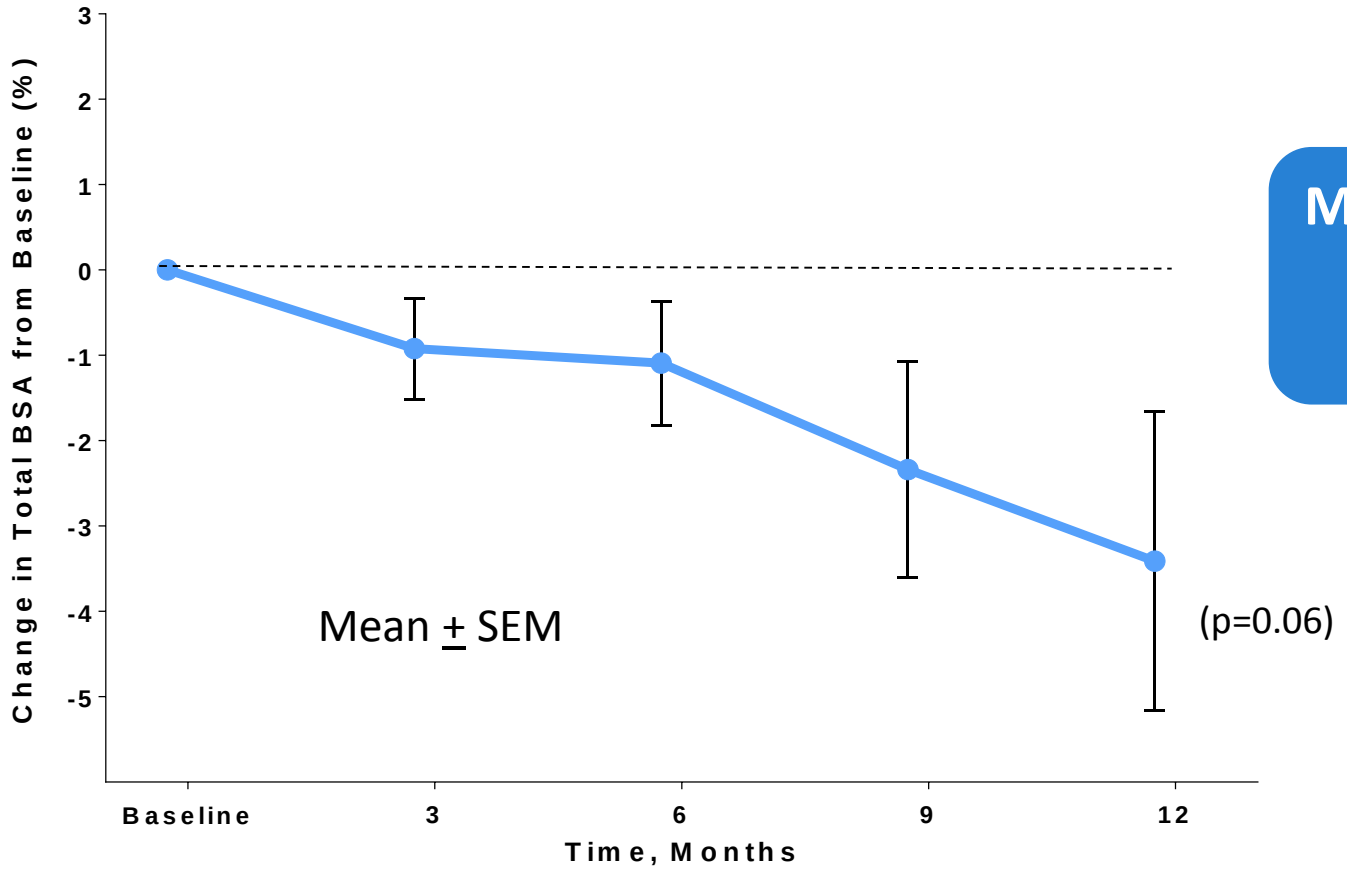
Phase 2b Efficacy and Safety Results Summary

- Efficacy
  - Treatment with the SD-101 formulation containing 6% allantoin (SD-101-6.0) demonstrated a higher rate of wound closure relative to both placebo treatment and treatment with the SD-101 formulation containing 3% allantoin (SD-101-3.0)
- Safety
  - The profiles of TEAEs for all treatment groups were similar
  - The 6% formulation is associated with an acceptable safety profile for the Phase 3 program

Key Learning Points For Phase 3 Study

- SD-101 6% concentration selected for Phase 3 study based on Phase 2b dose response
- Subgroup analysis indicates reduction of placebo response in patients with wounds ≥ 10 cm2
  - Complete target wound closure by 2 months
    - SD-101 6%: 50% (n= 4) vs. Placebo (SD-101 0%): 12.5% (n=8)
- Wound closure at Month 2 (vs. Month 1) is optimal time to measure primary endpoint
- Greatest difference between SD-101 6% and Placebo is at Month 2

Total Body Surface Area (BSA) Affected by Wounds/ Lesions Decreased with Time

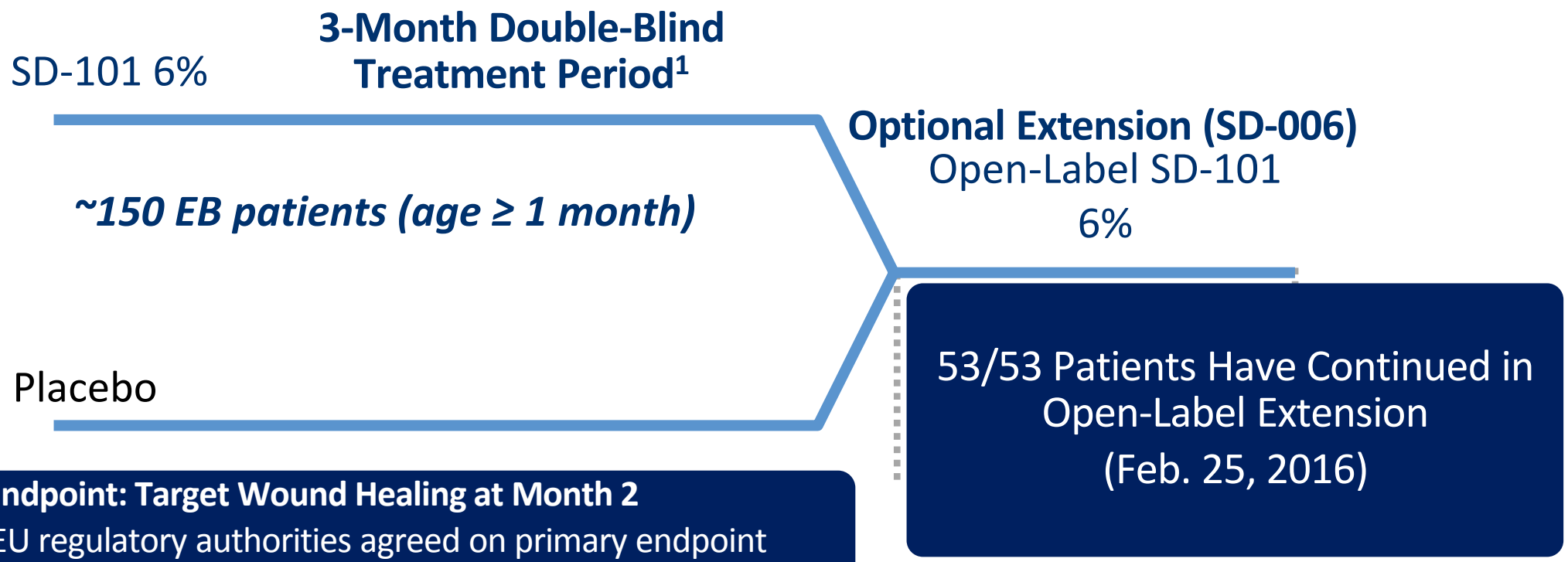


Mean Absolute Change to Month 12 (95% CI): -3.41% (-7.0, 0.2)

BL	M3	M6	M9	M12
n=42	n=37	n=33	n=30	n=28

Note: Baseline BSA for entire group = 11.3; Baseline BSA for group at 12 mos. = 10.9

Phase 3 Initiated in 2Q15 and ~50% Enrolled
Top-Line Data Expected 2H16



Primary Endpoint: Target Wound Healing at Month 2

- US and EU regulatory authorities agreed on primary endpoint
- Baseline wound: Chronic (≥ 21 days), size ≥10 cm^2

Secondary Endpoints Include

- Time to target wound closure
- Change in Body Surface Area (BSA) of lesions and blisters

[1]Assessments: 0, 14, 30, 60, 90 Days. 1:1 randomization, daily topical application

Study Design Incorporates Key Learning Points from Phase 2b Study

3-Month Double-Blind Treatment Period

SD-101 6%

Optimal concentration

~150 EB patients (age ≥ 1 month)

Sample Size (p ≤ 0.05 if treatment difference ~17% or greater)

Placebo

Optional Extension (SD-006)

Open-Label SD-101 6%

53/53 Patients Have Continued in Open-Label Extension (Feb. 25, 2016)

Primary Endpoint: Target Wound Healing at Month 2

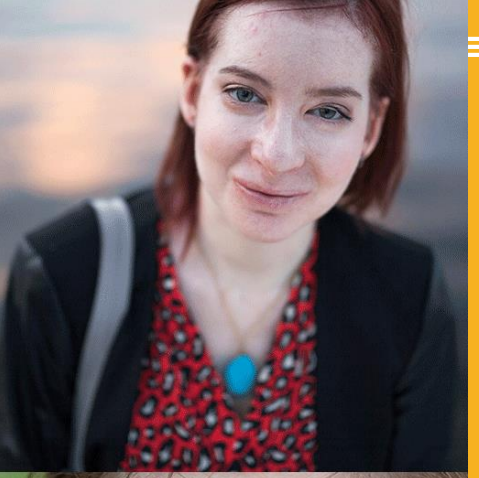
- US and EU regulatory authorities agreed on primary endpoint
- Baseline wound: Chronic (≥ 21 days), size ≥10 cm^2

Secondary Endpoints Include

- Time to target wound closure
- Change in Body Surface Area (BSA) of lesions and blisters

Increases Ability to Distinguish SD-101 vs. Placebo[1]

[1]Complete target wound closure in patients with target wounds ≥ 10 cm^2 at Month 2 in Phase 2b: SD-101 6% - 50% (n= 4) vs. Placebo - 12.5% (n=8)



Study 003 Acknowledgments

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Patients and their families

Investigators:

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- John Browning, MD
- Robert Sidbury, MD
- Rummana Aslam, MD

Study Site Staff

EB patient organizations