# Amicus trials - The clinical development of SD 101 in EB treatment

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# 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

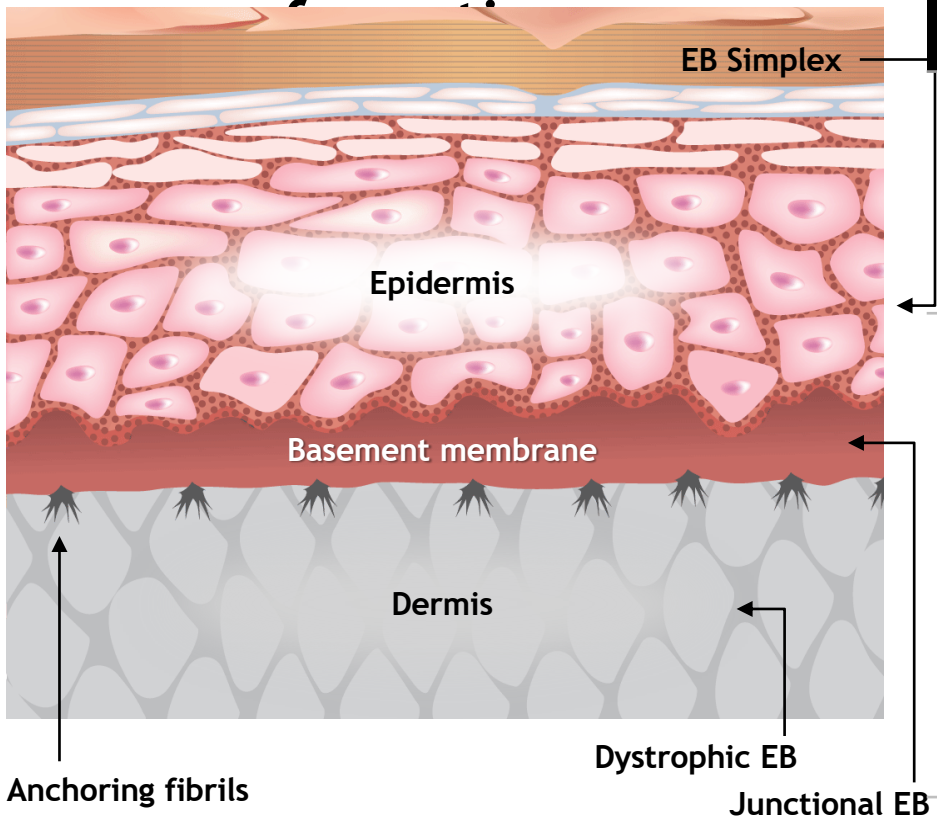
Disfiguring, excruciatingly painful, and can be fatal

Given few treatment options, any reduction in disease signs and symptoms would be considered important

30,000 – 40,000 diagnosed patients in major global regions

## Skin structure

### Sites of primary blister




Source: Adapted from DebRA

## EB Types

### Represent ~99% of EB Population

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

In 2013, SD-101 became one of the first drug candidates to receive Breakthrough Therapy designation from U.S. Food and Drug Administration (FDA) for the treatment of patients with EB. SD-101 also has orphan drug designation from the FDA and European Medicines Agency (EMA).

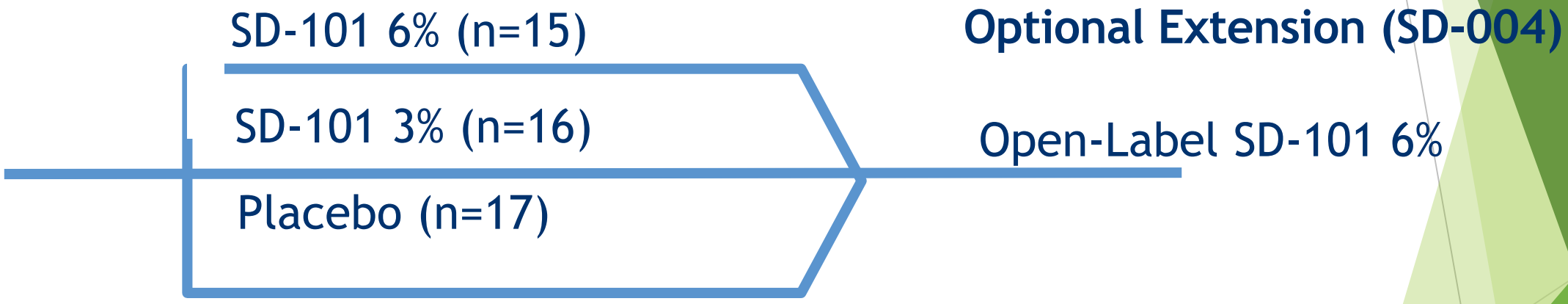
| | |
|---|---|
| Active Ingredient & ROA | Proprietary topical cream containing 6% allantoin, applied to entire body once daily |
| Proposed Indication | All major EB types (Simplex, Dystrophic, Junctional) |
| Development Phase -Now - | Phase 3 registration study (SD-005) ongoing |
| Proposed MOA* | 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

# Phase 2b Design (Study 003)

## 3-Month Double-Blind Treatment Period[1]

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




**42/44 Patients entered extension study**

**$400K FDA Grant for Extension Study**

# Phase 2b Design (Study 003)

## 3-Month Double-Blind Treatment Period[1]

**Primary Efficacy Endpoint: Target Wound Healing at 1 month**

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)

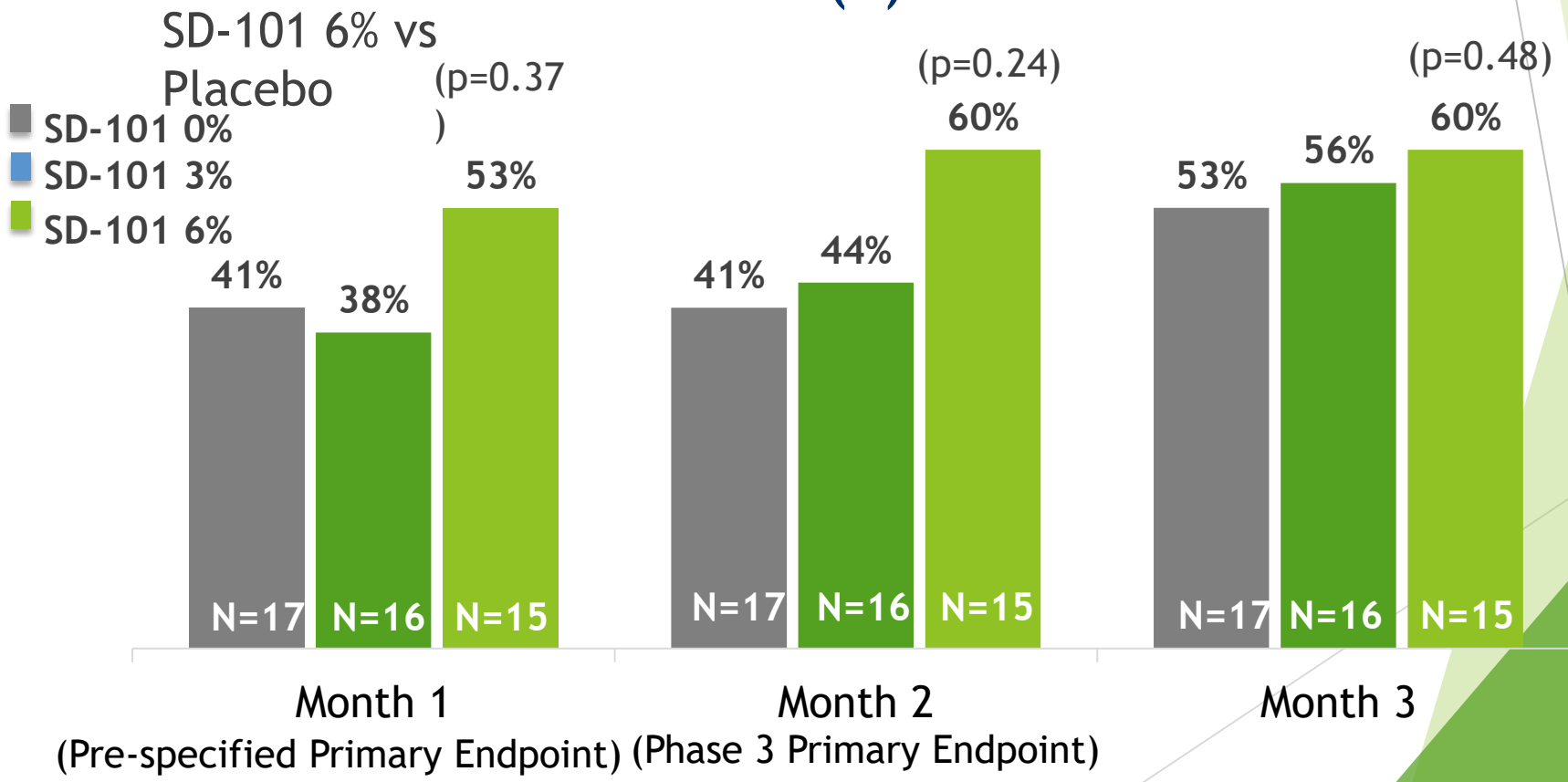
# Study 003

- 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)

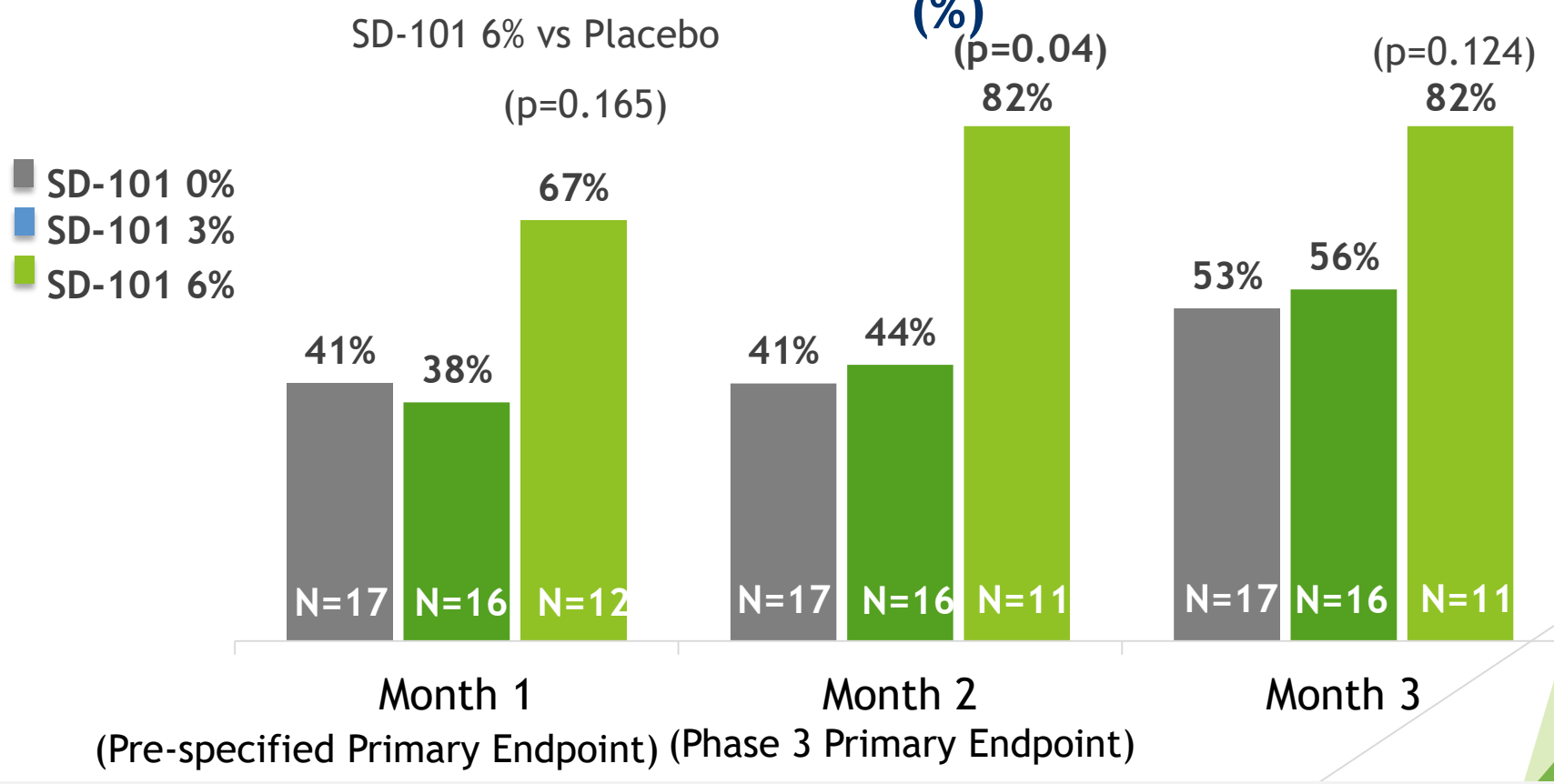
### Proportion of Complete Target Wound Closure (%)



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

## Evaluable Population[1] (n=45)

### Proportion of Complete Target Wound Closure (%)

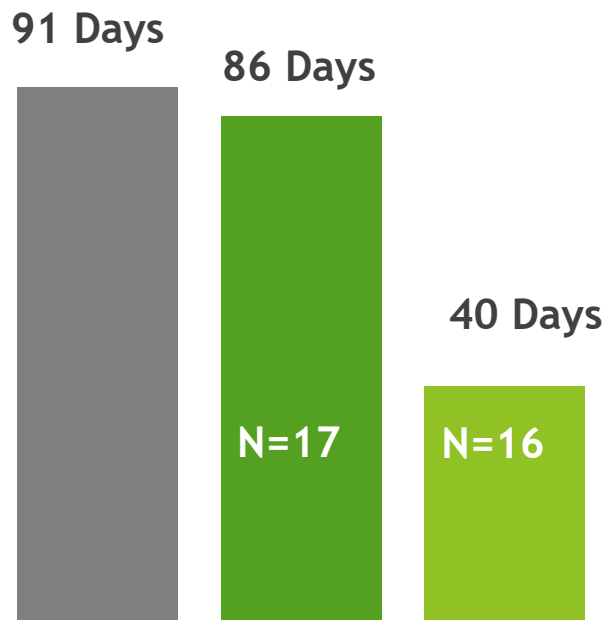



1. Excluded from Evaluable population: 1 patient (due to lost to follow-up), 2 patients (did not have single identified and qualified target lesion). 1 additional patient lost to follow up after Month 1 visit and is excluded from target wound assessment at later time points

# 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)

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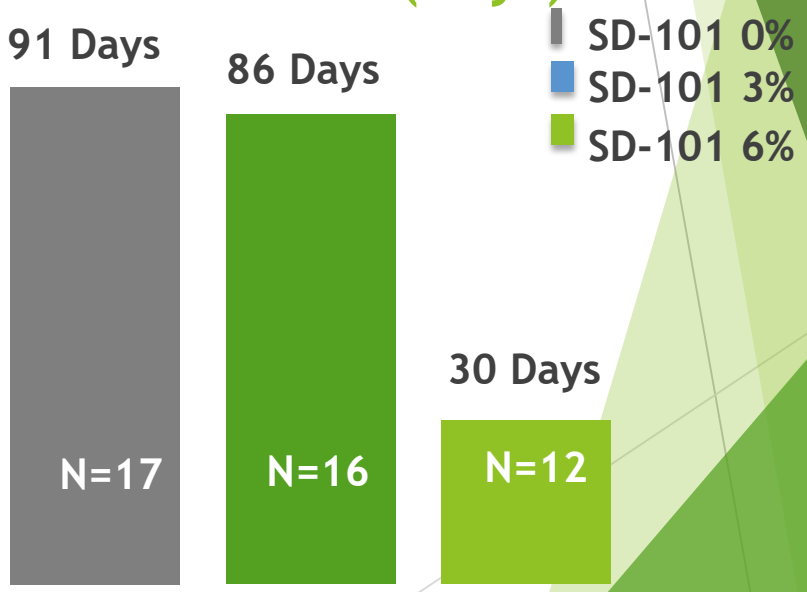


# Adverse Events Similar Across Placebo, SD-101 3%, and SD-101 6%

- 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

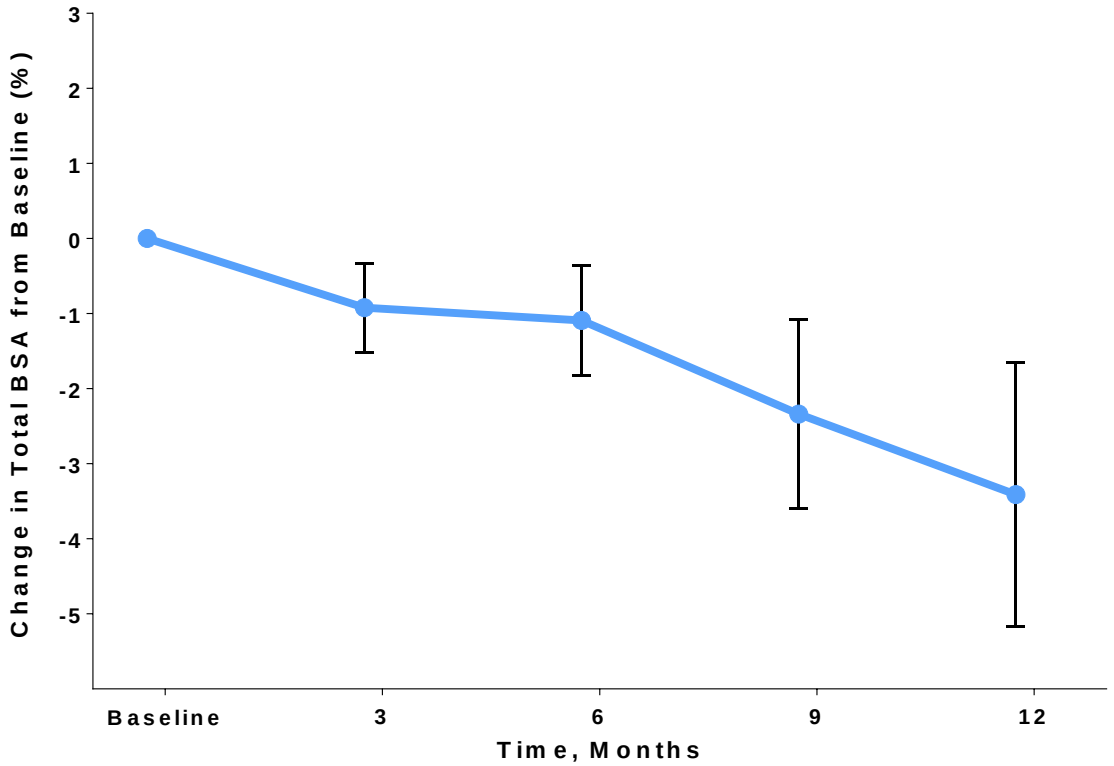
- The profiles of TEAEs for all treatment groups were similar
- The 6% formulation is associated with an acceptable safety profile for the Phase 3 program

# 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 $cm^2$
  - 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

# EXTENSION STUDY: Phase 2b Extension (Study 004) Results

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




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

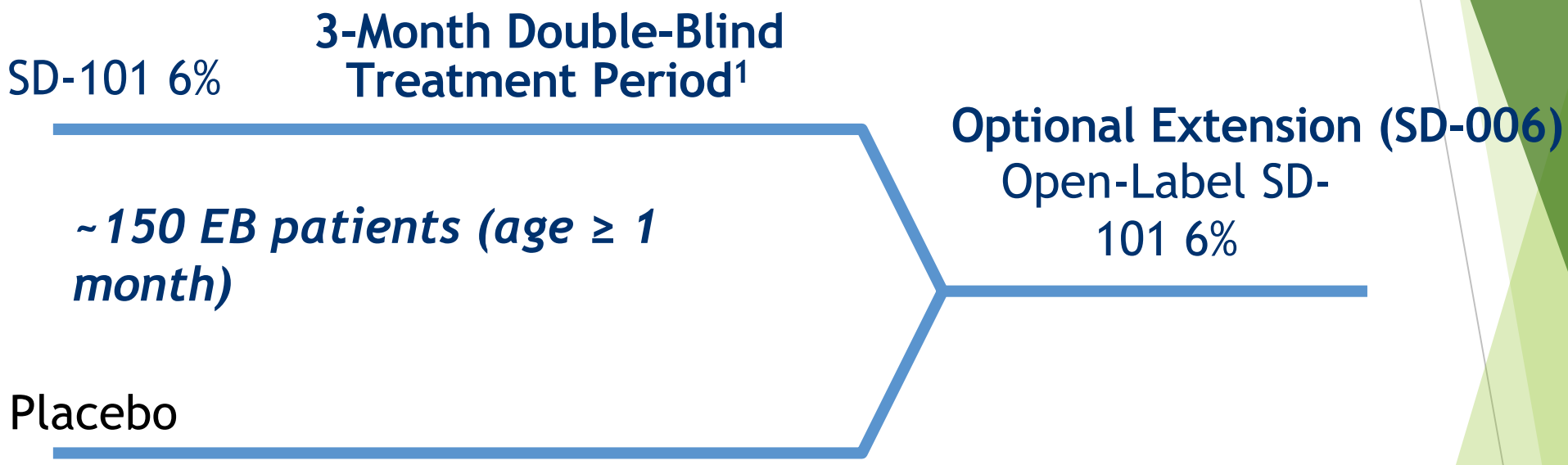
**Mean Absolute Change to Month 12 (95% CI): -3.41% (-7.0, 0.2)**

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

# SD-101: Phase 3 Study SD-005

- Study of Efficacy and Safety of SD-101 Cream in Patients with Epidermolysis Bullosa
- Status: Ongoing, currently recruiting patients 1 month and older with a diagnosis of Simplex, Recessive Dystrophic, or Junctional non-Herlitz EB who have a wound that meets specific study criteria as assessed by a healthcare professional.
- Design: A Phase 3, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of SD-101 Cream. SD-101 (6%) or placebo will be applied topically, once a day to the entire body for a period of 90 days. Patients who complete the study will be eligible to enroll in an open-label extension Study (SD-006).
- More information: www.clinicaltrials.gov: NCT02384460

# Phase 3 Initiated in 2Q15 and ~50% Enrolled




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

# Phase 3 Initiated in 2Q15 and ~50% Enrolled

**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

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