

Improving Lives of People with Rare Diseases



Our Mission

Paradigm Therapeutics is dedicated to the development of SD-101 (Zorblisa™), which is an innovative whole body topical therapy for people living with the rare disease, Epidermolysis Bullosa (EB), a devastating disorder for which there is no effective treatment

A Late-Stage Rare Disease Company



Zorblisa™
(allantoin)



Singular focus on rare diseases with significant medical need

Initial disease focus, EB, has no approved whole body treatment options across all EB subtypes

No therapies approved allowing treatment at birth

Demonstrated robust efficacy and safety

Convenient once daily, topical administration

Zorblisa™ positioned to be first-ever whole body treatment for all EB subtypes

Previous “Breakthrough Therapy Designation” in US

Orphan drug designations in US and EU

Small focused field sales force needed for specialty market

Proven team of development and scientific leaders

Deep and extensive relationships with EB experts and patient community

Investment Highlights: Zorblisa™ (SD-101)

The Only Full Body EB Treatment Across All Subtypes

Treatment of EB is a significant unmet medical need

- EB is a severe, chronic **genetic disease** with **no FDA approved whole body treatment** across all subtypes
- Prevalence estimated at 500k WW; 20-40k U.S.; 50-80k EU; 1-5k Japan
- Palliative treatment, including bandaging, creates a significant burden for families and caregivers (\$80k+/ month, excluding hospitalizations)

Zorblisa^R has demonstrated robust efficacy and safety

- Zorblisa™ (SD-101) is a proprietary topical therapy for treating the entire skin surface wounds and blisters associated with EB
- Demonstrated clinically significant efficacy in treating all EB subtypes (total EB patients = 217), with an excellent long term safety profile – **96+% of patients continued open label safety studies with Zorblisa™**
- **Only full body topical** therapy developed for treatment of all wounds and lesions (locally delivered to skin with no systemic absorption) - other therapies in development or approved only treat a single wound

Defined regulatory pathway

- First biotech drug to previously receive FDA breakthrough designation
- Previously granted orphan designation in US and EU, providing data protection for 7.5 and 12 years, respectively
- Orphan designation to be granted in Japan, will provide 10 years data protection

Commercialization strategy aided by physician concentration and patient advocacy

- Robust patient registries and well-networked patient advocacy groups will facilitate an effective commercial launch
- Highly concentrated prescriber base and centers of excellence

Experienced Leadership Team with Extensive Global Development Experience



Robert Ryan, PhD
Chief Executive Officer

Founder & CEO of Innova Therapeutics and Former Co-Founder and CEO of Scioderm. Former Managing Director of Celtic Pharma and Celtic Therapeutics, Board Member debra



Ronald V. Nardi, Ph.D.
EVP Development

35+ years experience in drug discovery/development and regulatory affairs, Operational and management R&D experience in large pharma organizations and small/medium sized companies including start-up/biotechnology firms



Michael Zimmer, MBA
Chief Financial Officer

Highly experienced executive brings 30 years of experience as a business leader in various roles including Finance, Accounting, Operations, Supply Chain, Business and Employee Development



Willistine Lenon
EVP Clinical Operations

Highly experienced Clinical Operations Executive with 29+ years in the field of clinical research, including senior roles at major CRO and pharmaceutical companies



Steve Cole
Head of BD and Licensing

Highly experienced Business Development/Licensing executive with 40+ years of global industry experience.



Epidermolysis Bullosa (EB)

“The worst disease you’ve never heard of¹”



¹ DEBRA America

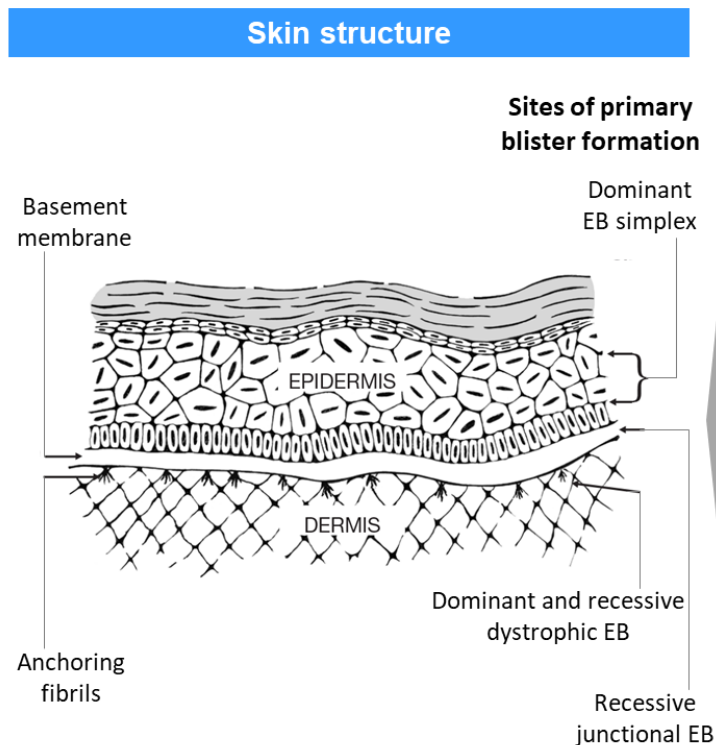
- **Epidermolysis Bullosa (EB) is a rare genetic disease of connective tissue, manifested by defective or deficient anchoring fibrils which provide structural support primarily in the skin**
- Manifested by defective or deficient anchoring fibrils - primarily in skin
- Characterized by extreme fragility of the skin
- Typically manifests at birth
- Disfiguring and very painful
- Mildest friction damages skin causing severe blistering and wound formation
 - Itching exacerbates wounds and healing
 - Wounds often become chronic; result in significant scarring
- Life altering; results in inability for patients to thrive
- Disease unknown until birth; can be fatal (typically due to sepsis)

EB is an Orphan Disease in the U.S and E.U. and an Ultra-Orphan Disease in Japan

Official estimates of prevalence are increasing as the disease becomes better understood

- **US: Est. 20,000 - 40,000 current cases (comparable to Cystic Fibrosis)**
 - Debra (Dystrophic Epidermolysis Bullosa Research Association of America) web site: 30,000
 - Stanford University EB web site: 25,000 – 50,000
 - EBMRF (EB Medical Research Foundation) – “Estimates indicate that as many as 100,000 Americans suffer from some form of EB.”
- **EU: Est. 50,000 to 80,000 current cases**
 - Gabriella Pohl-Gubo (5th International Conference on rare diseases-Krakow 2010)
 - Prevalence estimates in Northern Europe
 - Northern Ireland ~ 44/M (Covello et al. J INV DERM, 1998)
 - Scotland ~ 49/M (Horn et al. BRIT J DERM, 2008)
- **Japan: 1,000 – 5,000**
 - ~1,000 (Study Group for Rare Intractable Skin Diseases in 1994)
 - “at least 1,000 severe cases and likely thousands more” (Debra Japan)
- **Worldwide prevalence estimated at 500,000 patients**

There are Three Main Subtypes of Epidermolysis Bullosa* - All Need Treatment



Source: Adapted from DEBRA America

EB subtypes

Subtypes	Symptoms	Frequency	Mortality risk
Simplex	<ul style="list-style-type: none"> ➤ Blistering on hands and feet (localized) ➤ Blistering all over body (generalized) ➤ Contraction of joints ➤ Fusion of fingers and toes 	40 - 70%	
Dystrophic	<ul style="list-style-type: none"> ➤ Contraction of mouth membranes ➤ Narrowing of esophagus ➤ Possibility of skin cancer 	25 - 50%	
Junctional	<ul style="list-style-type: none"> ➤ Marking and damage to skin or face ➤ Internal blistering of oral tracts ➤ Extensive blistering all over body ➤ Blistering of membranes of internal organs ➤ Severe complications can often become lethal 	5 - 20%	

*Kindler EB is a very rare 4th type of EB (<1%)

Mellerio, Jemima E. et al. Mapping the burden of severe forms of epidermolysis bullosa – Implications for patient management. JAAD International, Volume 11, 224 - 232

Non-confidential

EB Patients Receive Care at Centers of Excellence...

There are comprehensive EB pediatric/adult clinics worldwide including a newly created EB clinic in Abu Dhabi



Children's Hospital Colorado



COLUMBIA UNIVERSITY
MEDICAL CENTER
Discover. Educate. Care. Lead.



LANDESKRANKENHAUS SALZBURG
UNIVERSITÄTSKLINIKUM
DER PARACELBUS MEDIZINISCHEN PRIVATUNIVERSITÄT



HOKKAIDO UNIVERSITY
Graduate School of Medicine



STANFORD
SCHOOL OF MEDICINE



- There are a concentrated number of EB specialized research hospitals with large, identified patient populations
- DEBRA, the worldwide patient advocacy group, maintains large databases of patients

...However, There are Presently No Cures and Primarily Palliative Treatment



Source: DEBRA America

- **Overall treatment goals are skin protection to minimize blister and wound formation, and infection minimization**
- **The principal treatment, usually in a home care setting, involves daily wound care, protective bandaging and pain management**
 - Primary goals are protection of skin from further injury and infection minimization
 - Management of severe and debilitating wound pain and itching
- **Surgery can become necessary and varies among patients according to phenotype**
 - Dilation of the esophagus to relieve dysphagia
 - Repair of hand / foot deformities
 - Typically not effective
 - Removal of any squamous cell carcinoma that develops
 - Typically still lethal
- **EB creates tremendous financial burden with limited to no treatment effect**

Zorblisa™ Overview

Pharmacological Actions of Active: Multi-Faceted

➤ Accelerates wound healing by promoting formation of granulation tissue

- Dose-related stimulation of collagen deposition early in wound healing, accelerating healing with no keloid formation (Araujo *et.al.* 2010, 2012).
- Effective in fibroblastic migration and synthesis of extracellular matrix during wound healing, stimulation of granulation tissue formation in ulcers, including epithelialization (Meixell *et al.* 1966; Margraf 1977).

➤ Bacteriostatic, Bactericidal, and Effective in Removing Necrotic Tissue

- Chemical debridement *via* promotion of leukocyte migration and phagocytosis (MacAlister CJ 1936; Margraf *et al.* 1977; Yakugaku Zasshi 1998; Meixell 1966).
- Direct bacteriocidal action on various bacteria *in vitro*, including *Staphylococcus aureus* and *E. Coli* (Settle 1969).

➤ Keratolytic activity

- Removes calluses and other forms of hyperkeratinization by dissolving “cement” holding cornified cells together – loosening of desmosomes (protein bridges) (Fisher 1981; Cajkovac *et al.* 1992; Mecca 1976).

➤ Anti-inflammatory Effects

- Following leukocyte stimulation, migration, and phagocytosis, the active moiety appears to reduce the inflammatory response at the site of the wound. Demonstrated earlier reduction in inflammatory infiltrates *versus* control in rat wound model. (Araujo *et al.* 2010, 2012).
- In cases of skin challenge from mechanical, chemical, or UV irradiation – decrease in erythema (Henning 2001).

Zorblisa™ (SD-101) will be the Only Whole-Body EB Treatment for All Subtypes

- **Zorblisa™ is a proprietary new molecular entity (NME) which has completed Phase 3 development in the US and EU**
 - Topical fast dissolving cream
 - Demonstrated efficacy and excellent safety in Phase 2a, Phase 2b, and Phase 3 trials
 - No systemic absorption, locally delivered
 - Zorblisa™ previously received orphan designation for the US and EU, and would qualify in Japan **(10 years exclusivity)**
 - US data exclusivity for orphan designation will be for 7.5 years
 - Approved PIP in Europe - 12 years data exclusivity with defined registration path
 - No pathway for generic drugs for non-systemic therapeutics post expiration of exclusivity
 - Worldwide commercialization rights



Comparison of Zorblisa™ versus Approved/ Late-Stage EB Programs in Development

Key Differentiating Characteristics

	Paradigm (SD-101)*	Amryt**	Castle Creek	Krystal **	Abeona
Patient Population	Simplex, Junctional and Dystrophic	Dystrophic, Junctional	Recessive Dystrophic only	Recessive Dystrophic only	Recessive Dystrophic only
Treatment Area	Whole body	Applied to multiple wounds	Single wound	Single wound	Single wound
Treatment Benefit	Healing of lesions and wounds on whole body in addition to healing of target wound	Healing of only target wound	Healing of only target wound	Healing of only target wound	Healing of only target wound
Type of Therapy	Cream locally delivered across various skin layers without systemic absorption	Birch bark extract in sunflower oil	Fibroblast cells transduced with lentivirus vector carrying COL7A1 ex vivo to express COL7.	"Replication-defective", non-integrating herpes viral vector engineered to deliver synthetic human COL7A1 gene	Keratinocytes cultured from skin, transduced with retrovirus containing full length COL7A1 ex-vivo; epidermal sheets stitched onto patient
Source	Synthetic small molecule	Birch Bark extract	Autologous fibroblasts	Keratinocytes	Autologous skin biopsies
Administration	Topical	Topical	Intradermal Injection	Topical	Transplantation

* Benefits specifically for SD-101 (Zorblisa) compared to competitors in **"bold"**

Amryt/Chiesi (Filsuvez) approved in US and EU, Krystal (Vyjuvek) and Abeona (Zevaskyn) approved in US

Comparison of the Zorblisa™ Product Characteristics Versus Approved Therapies Label Information

	Zorblisa™	Filsuvez® - Approved	Vyjuvek™ - Approved	Zevaskyn - Approved
Patient Population	Simplex, Junctional and Dystrophic	Junctional, Dominant and Recessive Dystrophic	Recessive Dystrophic only	Recessive Dystrophic only
Treatment Area	Whole body	Instructed to treated up to four wounds but one wound identified as target wound for primary endpoint assessment	Single wound	Single wound
Treatment Benefit	Healing of lesions and wounds on whole body in addition to healing of target wound	Healing of only target wound	Healing of target wound	Healing of target wound
Type of Therapy	Topical cream locally delivered across the entire skin surface	Birch bark extract in sunflower oil gel applied to selected wounds	“Replication-defective”, non-integrating herpes viral vector engineered to deliver synthetic human COL7A1 gene	Keratinocytes cultured from skin transduced with retrovirus containing full length COL7A1 ex-vivo, epidermal sheets stitched onto patient
Source	Synthetic small molecule	Birch Bark extract	Keratinocytes	Autologous skin biopsies
Administration	Topical daily or during bandage changes – Chronic therapy which does not require bandaging after application	Topical treatment every one to four days – requires treatment area to be bandaged	Topical treatment on a single wound once per week until healed Product must be applied by medical professional and requires bandaging of the treatment area	Transplantation

Pricing Comparison

Zorblisa anticipated pricing (TBD): Daily treatment of entire skin surface of EB patients across all subtypes

- Estimated pricing of \$100k per year or less for treatment of the entire skin surface including all wounds and lesions

Filsuvez (Chiesi): FDA and EU approved with minimal treatment benefit at 45 days in only **a wound in RDEB only** (approved for Junctional but placebo response better than treatment response)

- US pricing: estimated \$80K per year for one wound
- EU pricing: UK and Germany \$65K per year for one wound

Vyjuvek (Krystal): FDA approved for treatment of **a single wound in RDEB only**

- US pricing: \$660K for 6 months one a week treatment of one wound, \$1M+ for one year treatment

Zevaskyn (Abeona): FDA approved **autologous skin** (size of credit card) to cover a single wound in RDEB only

- US pricing: \$3.1M estimated for yearly pricing for reengineered skin for grafting.

Phase 2a investigator Study (Dr. Paller) Results Simplex, Junctional and Dystrophic EB Patients

Individual Patient Data (Patient 2) – Impact on Hyperkerolytic Lesions

Baseline Characteristics: 4 y.o. girl with Simplex EB – 67% body surface area coverage with blisters and/or erosions

Visits 2 (month 1) and 3 (month 2)

Physician Global Assessment of Improvement – 75% improvement

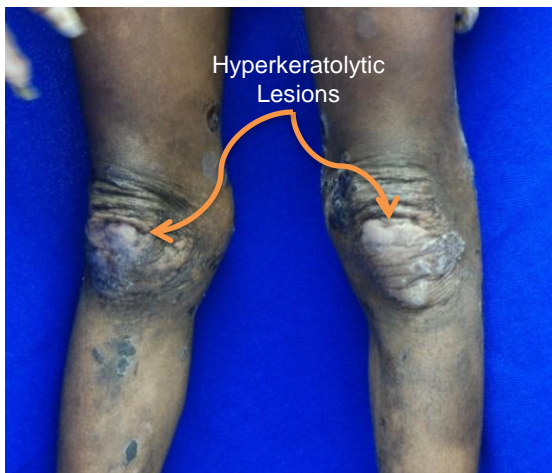
Body Surface Area affected down to 17.5% month 2 (73% reduction compared to baseline)

12 cm² target lesion completely closed at month 1

Visit 4 (month 3)

Body Surface Area affected down to 11.2% (83% reduction compared to baseline)

New lesion treated starting after month 1 visit – 29.3 cm², completely closed



Individual Patient Data (Patient 3)

Baseline Characteristics: 1 y.o. girl with Simplex EB – 49% body surface area coverage with blisters and/or erosions

Visits 2 (month 1) and 3 (month 2)

Physician Global Assessment of Improvement – 25% improvement month 1, 75% improvement month 2, compared to baseline

Body Surface Area affected down to 12% month 2 (75% reduction compared to baseline)

Visit 4 (month 3)

Physician Global Assessment of Improvement – 25% improvement compared to baseline

Body Surface Area affected 26%
(47% reduction compared to baseline)

14.4 cm² target lesion completely closed

Baseline Picture



Pictures following 2 months treatment



Individual Patient Data (Patient 3)

Baseline Picture R Shoulder



R Shoulder following 2 months treatment



Baseline
Picture of
Back



Back following 2
months treatment



Individual Patient Data (Patient 7)

Baseline Picture Shoulder



Picture following 2 month treatment



Phase 2b Studies

Phase 2b Study (SD-003) Design*

Study design	
Design	Double-blind, randomized, parallel group, placebo-controlled
Treatments/Groups	48 EB patients divided equally into 1 of 3 treatment arms: <ul style="list-style-type: none"> • Placebo • Zorblisa-3.0 (3%) • Zorblisa-6.0 (6% active)
Dosing/Duration	Topical application QD (total body SA)/3 months
Randomization	Balanced (1:1:1)
Target lesion	Chronic (21 days or longer) $\geq 5 \text{ cm}^2$ and $\leq 50 \text{ cm}^2$
Assessments	0, 14, 30, 60, 90 days
Efficacy	Primary Endpoint - Target Lesion Healing <ul style="list-style-type: none"> • Endpoint agreed by U.S. and E.U. Regulatory Authorities Secondary Assessments <ul style="list-style-type: none"> • Change in body surface area coverage of lesional skin • Itching • Pain
Safety	Adverse events

*All patients offered opportunity to continue on open label therapy (SD-004) after completion of SD-003 study participation

95% of patients participated in open-label extension study

Zorblisa™ Phase 2b (Study SD-003) Demonstrated Improvement in Wound Closure and Reduction in Whole Body Coverage in Lesions

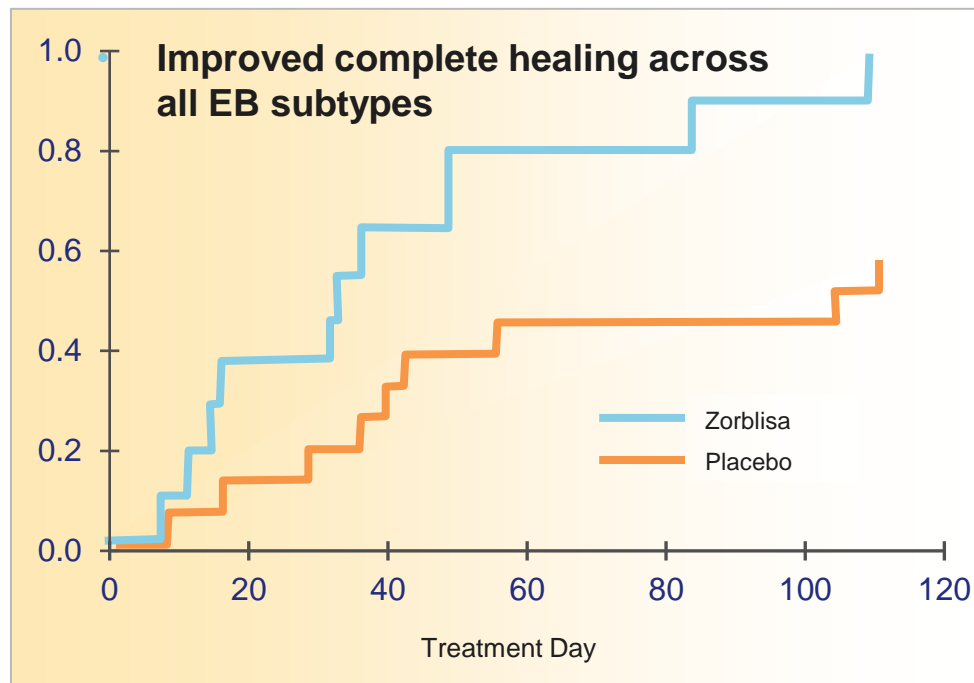
Wound-healing time reduced by 2/3 among patients receiving Zorblisa^R

- Median time to complete healing:

Zorblisa – 31 days

Placebo – 91 days

- Proportion of complete target wound closure greater in Zorblisa-treated group versus placebo
 - >70% improvement in Zorblisa group relative to placebo
- Full body coverage in lesion skin reduced by 28% by Month 3 in the Zorblisa-treated patients compared to patients on placebo (5.75% reduction)



Phase 2b Study (Study SD-003) Patient Picture Examples

- Zorblisa™ patients demonstrate visible wound closure in short periods of time
- Note reduction in inflammation in addition to rapid wound healing



Excellent Safety Profile for Zorblisa™ (Studies SD-003 and SD-004)

SD-003 Phase 2b Study

- Treatment-emergent adverse events (TEAE) similar across treatment groups, including placebo group
- Skin infections reported were higher in the placebo group (5.9%) compared to the Zorblisa-treated group (none reported)
- No deaths in the trial and no severe related or unrelated TEAEs
- No serious adverse events were reported in the Zorblisa^R group

SD-004 Phase 2b Open Label Extension Study

- 42 of 44 patients (95%) completing Study SD-003 enrolled in the open label extension study (SD-004)
 - Study SD-004 patients all used Zorblisa™ daily, many in excess of 2 years
 - Long term safety treatment with Zorblisa™ in subjects with Simplex, Junctional and Recessive Dystrophic EB was considered safe and well tolerated

Phase 3 Studies

Phase 3 Study (SD-005) Design Description

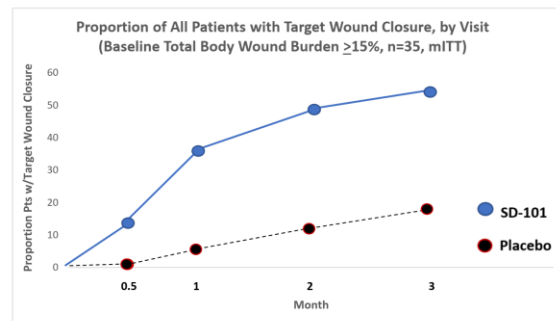
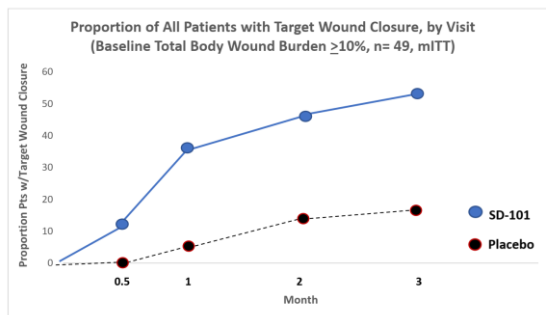
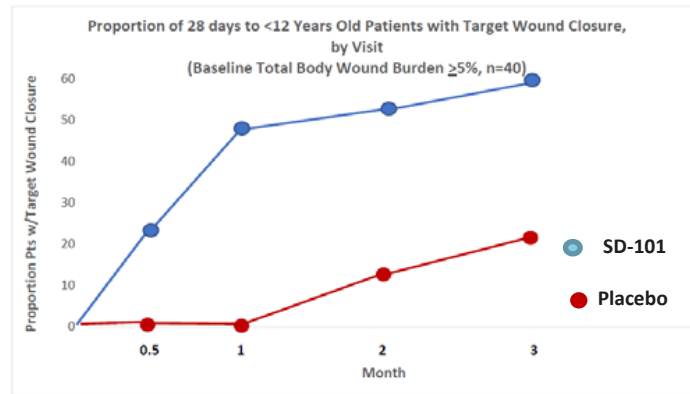
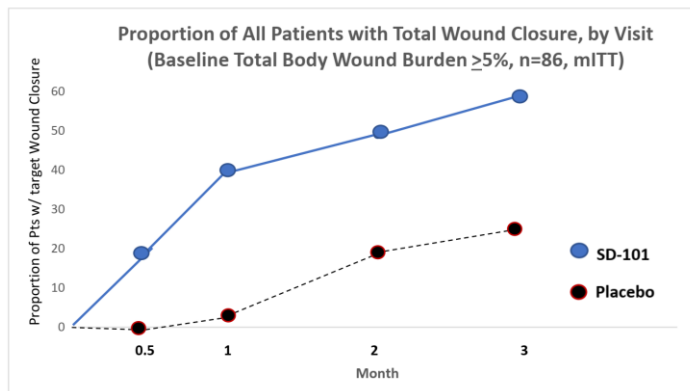
Design	Double-blind, randomized, parallel-group, placebo-controlled dose-response study – 13 sites
Treatments / groups	<p>130 EB patients (expanded to 169 by Amicus) 1 month or older (Simplex, RDEB, Junctional (Non-Herlitz)) divided equally into 1 of 2 treatment arms:</p> <ul style="list-style-type: none"> ➤ Placebo ➤ Zorblisa[®] (6% active)
Dosing / duration	Topical application QD (total body SA) / 3 months then eligible to continue on open label therapy (SD-006 study)
Randomization	Balanced (1:1)
Target lesion	Chronic (21 days or longer) ≥10 cm ²
Assessments	0, 14, 30, 60, 90 days
Efficacy	<p>Original Primary endpoint - target lesion healing <u>within 1 month of treatment</u></p> <ul style="list-style-type: none"> ➤ Regulatory-approved endpoint <p>Secondary assessments</p> <ul style="list-style-type: none"> ➤ Change in body surface area coverage of skin lesions and wounds ➤ Itching ➤ Pain

Safety

Adverse events

Non-confidential

Target Wound Closure in All Patients with Total Body Surface Area (BSA) Wound Burden at Baseline >5%, >10%, >15% Including Subset of High Risk Patients 28 days to <12 years old with More Extensive Baseline Total Body Wound Burden



Median Time To Target Wound Closure Faster with Treatment with SD-101-6.0 (Zorblisa™) Versus SD-101-0.0 (Placebo)

A key characteristic of a beneficial therapy for treating wounds in patients with EB is the ability to heal wounds quickly. SD-101-6.0 treatment has been shown in both the Phase 2 and Phase 3 double-blind studies to accelerate target wound closure faster than wounds that closed in patients receiving the placebo.

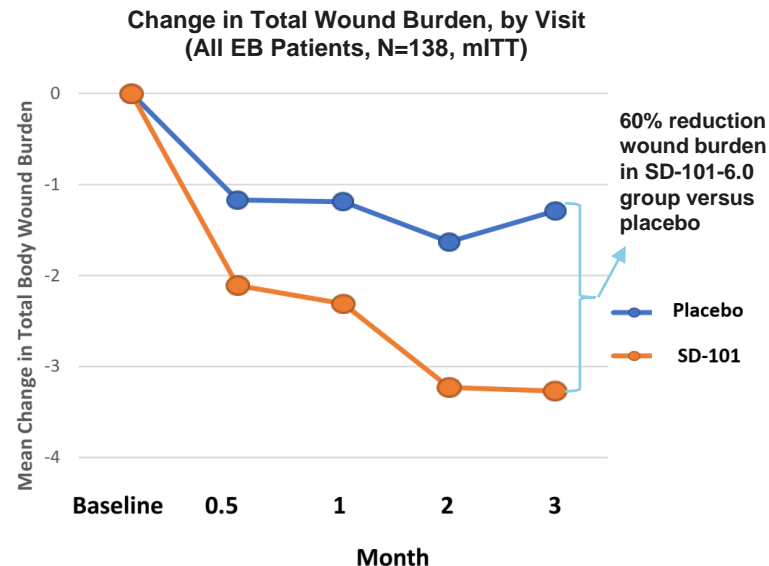
In the Phase 3 SD-005 Study, SD-101-6.0 was shown to accelerate target wound closure **faster** than wounds that closed in patients receiving SD-101-0.0 (placebo).

Median Time to Target Wound Closure (144 subjects)	
SD-101-6.0	Placebo
31 days	58 days

*Note: In the Phase 2 Study SD-003, median time to complete wound healing in the evaluable patient (EP) groups treated with **SD-101-6.0** was **29.5 days, respectively, versus 91 days in the SD-101-0.0 patients.***

Improvement in Whole Body Wound Burden Reduction with SD-101-6.0

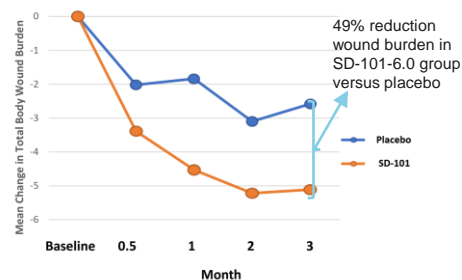
Total Body Surface Area (BSA) Wound Burden at Baseline – All Patients



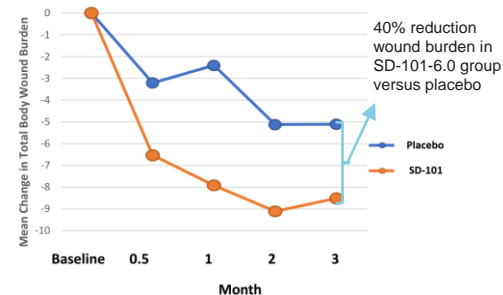
Note: In Phase 2b study full body coverage in lesion skin reduced by 28% by Month 3 in the Zorblisa-treated patients compared to patients on placebo (5.75% reduction)

Total Body Surface Area (BSA) Wound Burden at Baseline $\geq 5\%$, $\geq 10\%$, $\geq 15\%$

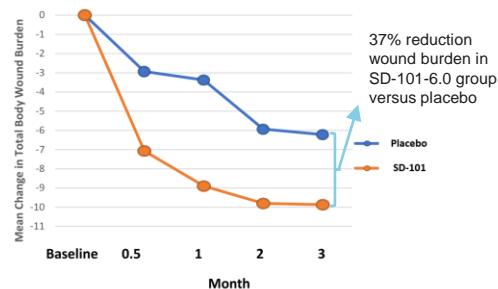
Change in Total Body Wound Burden, by Visit
(Baseline Total Body Wound Burden $\geq 5\%$, n=84, mITT)



Change in Total Body Wound Burden, by Visit
(Baseline Total Body Wound Burden $\geq 10\%$, n=46 mITT)



Change in Total Body Wound Burden, by Visit
(Baseline Total Body Wound Burden $\geq 15\%$, n=35 mITT)



48% Reduction in Infection Across the Whole-Body Skin Surface with SD-101-6.0 (Zorblisa™) Versus SD-101-0.0 (Placebo)

In the Phase 3 SD-005 study the **proportion of patients with whole surface skin infections as assessed by the principal investigator was statistically significantly lower in the SD-101-6.0 group versus the SD-101-0.0 group (18.3 versus 35%, P=0.026)** which translates to a **48% reduction** in whole body skin infections in the SD-101-6.0 group versus the SD-101-0.0 group.

Note: In the Phase 2b study SD-003 the proportion of patients with whole body skin infections was lower in the SD-101-6.0 group versus the placebo group (none reported in SD-101-6.0 group versus 5.9% in the SD-101-0.0 group.

Itch in Epidermolysis Bullosa has Been Rated as the Most Troublesome Symptom Change in Itching was a Secondary Endpoint in Phase 3 SD-005 Study

- In a survey of 40 adults with either of the three major EB types (EBS, JEB or DEB), **85% reported itch**, a prevalence similar to that found in atopic dermatitis (AD). Other aspects such as frequency, duration and severity were also comparable with those in AD. The highest prevalence was noted in individuals with **Junctional EB (100%) and Recessive Dystrophic EB (RDEB) (100%), followed by Dominant Dystrophic EB (87%) and EB Simplex (74%)**. Results were similar in a survey of 146 US patients of all ages and all EB types.
- **Itch was rated as the most troublesome symptom**, above pain, eating problems and wound infections. Its frequency increased with self-reported disease severity, being the highest in RDEB.
- Healing wounds and the surrounding skin, infected wounds and dry skin were significantly more itchy than non-wounded skin or scars, and the **incidence of pruritus was highest in body areas with the greatest number of wounds**.
- Itch was also ranked as the top concern in interviews involving 10 children with EB. Children with more severe disease ranked itch higher in their list of concerns. A Korean cross-sectional study of 13 patients with RDEB of severe or intermediate type also assessed pruritus using a visual analogue scale (VAS), with the mean score indication of severe itch.

Papanikolaou M, Onoufriadis A, Mellerio JE, Nattkemper LA, Yosipovitch G, Steinhoff M, McGrath JA. Prevalence, pathophysiology and management of itch in epidermolysis bullosa. Br J Dermatol. 2021 May;184(5):816-825. doi: 10.1111/bjd.19496. Epub 2020 Nov 29. PMID: 32810291.

Improvement in Itching Day 1 to 7

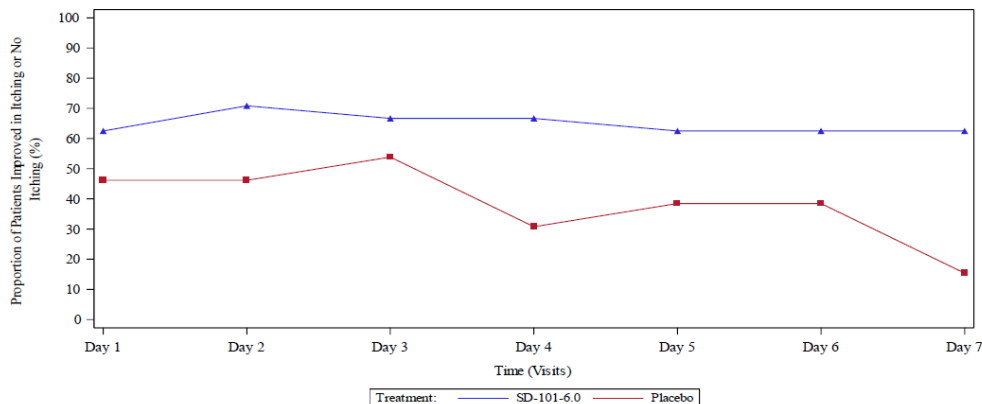
Patients with Total Body Wound Burden of $\geq 15\%$ at Baseline

(Change in Itching was a Secondary Endpoint in Phase 3 SD-005 Study)

Amicus Therapeutics
Compound: SD-101 Study SD-005

Page 1 of 1

Figure 14.2.16.1.1.5b
Improvement in Itching over Time (Baseline BSAI of Total Body Wound Burden $\geq 15\%$) (Day 1 to Day 7)
MITT Population



Proportion of Patients at Day 7 with Improved or No Itching

62.5%

15.4 %

Phase 3 Study Secondary Endpoint: Change in itching assessed at Week 1 (Day 7), compared to Baseline will be measured using the "Itch Man Pruritus Assessment Tool". For patients 1 month to 5 years of age itching will be assessed using caretaker's response and patients 6 years of age and older will self-report their itching assessments.

Note: Improved or no itching is an itching score reduction from baseline greater than or equal to 1 point on the scale or itching score of 0 at both baseline and post-baseline.

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Improvement in Itching Day 1 to 7

Patients with Total Body Wound Burden of $\geq 15\%$ at Baseline

(Change in Itching was a Secondary Endpoint in Phase 3 SD-005 Study)

Paradigm Therapeutics

Protocol Number: SD-101 Study SD-005

Table 14.2.16.1.1.2c
Logistic Regression for Improvement in Itching over Time (Baseline BSAI of Total Body Wound Burden $\geq 15\%$)
(mITT Population)

		Time: Day 7 (n=32)		
Factor	Factor Level		Odds Ratio (95% CI)	p-value
Treatment	SD-101-6.0 vs Placebo		8.335 (1.369, 50.756)	0.021
Baseline Itching Score			1.311 (0.723, 2.379)	0.373

Note: For this analysis Itching scores were categorized into two groups based on improvement: Improved or No Itching, and Not Improved. Improved is an itching score reduction from baseline greater than or equal to 1 point on the scale. The proportion of patients experiencing improvement in itching versus non-improvement (excluding missing) was compared between the two treatment groups for each visit using the logistic model with baseline itching score as covariate. In the case that complete separation and quasi-complete separation occurs from the logistic regression model as specified above, the explanatory variable causing the situation will be identified and excluded from the model. If the treatment factor is that variable, then the treatment effect will be tested using the chi-square test. Factor(s) with an asterisk (*) will be removed from the model due to the reasons above. p-value is from Type 3 Tests to present as overall p-value for each term in the model. Day 7 is not evaluated in this table because change in itching assessment at Day 7 is a key secondary endpoint and is evaluated in a separate table.

n is the number of patients who have itching assessments at each visit

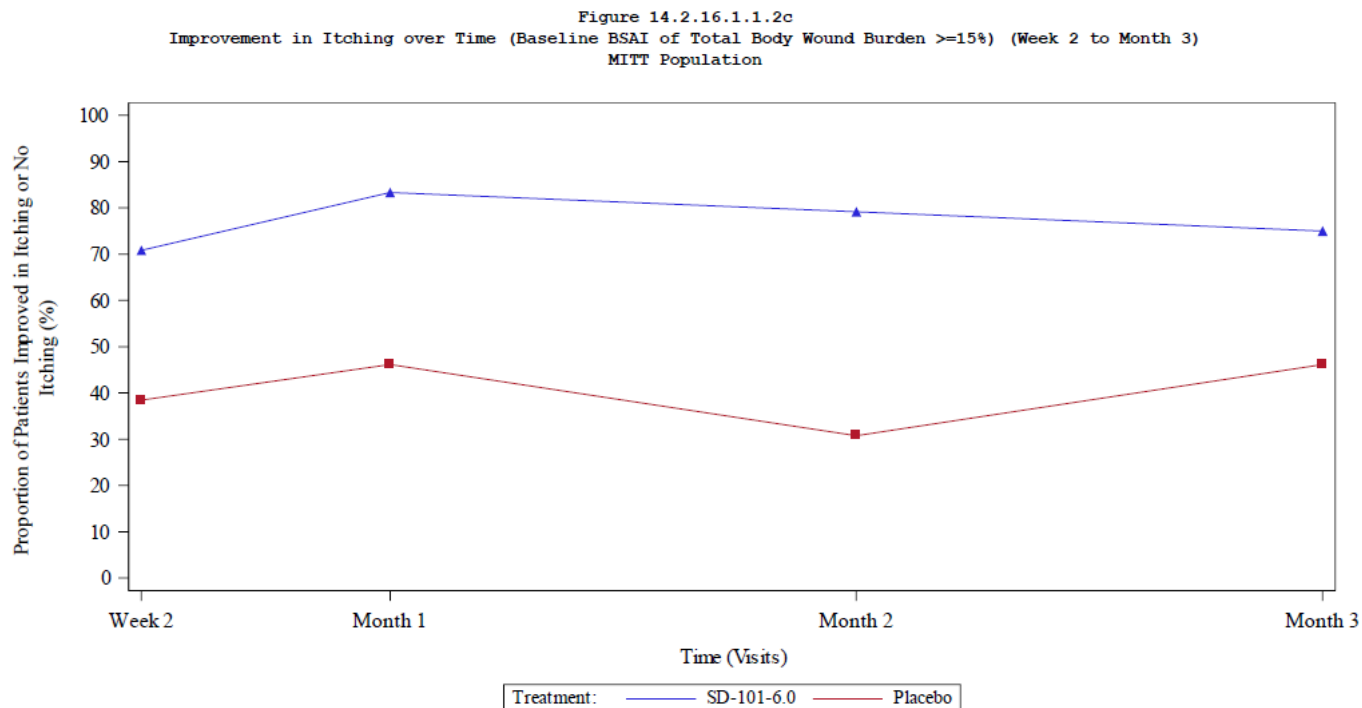
[1] EB type: Epidermolysis Bullosa type.

Source Data: Listing 16.2.4.1, Listing 16.2.6.3

Improvement in Itching Baseline to Month 3

Patients with Total Body Wound Burden of $\geq 15\%$ at Baseline

(Change in Itching was a Secondary Endpoint in Phase 3 SD-005 Study)

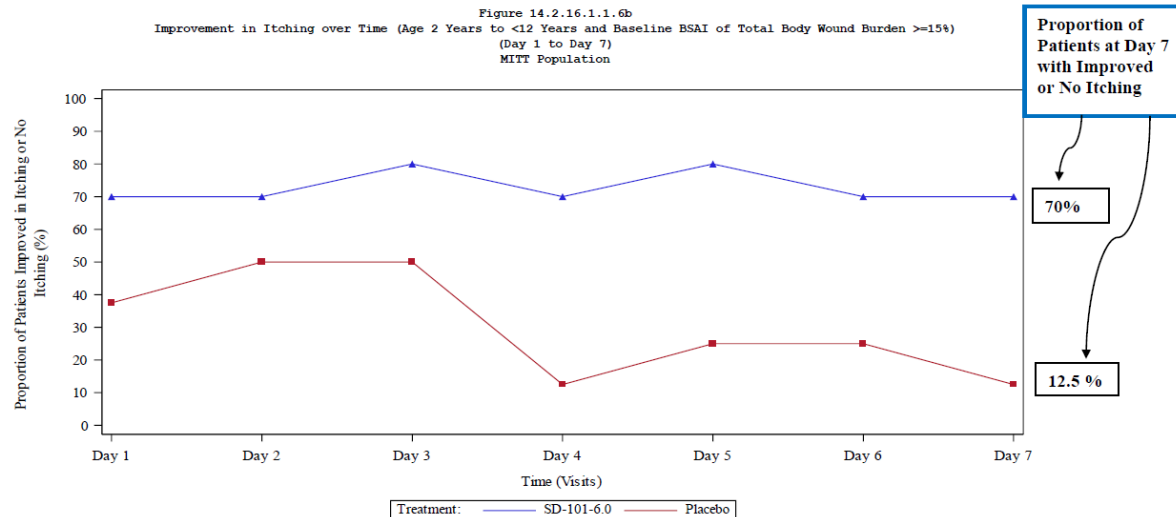


Improvement in Itching Day 1 to 7

Patients (2 to <12 Years Old) with Total Body Wound Burden of $\geq 15\%$ at Baseline (Change in Itching was a Secondary Endpoint in Phase 3 SD-005 Study)

Amicus Therapeutics
Compound: SD-101 Study SD-005

Page 1 of 1



Phase 3 Study Secondary Endpoint: Change in itching assessed at Week 1 (Day 7), compared to Baseline will be measured using the "Itch Man Pruritus Assessment Tool". For patients 1 month to 5 years of age itching will be assessed using caretaker's response and patients 6 years of age and older will self-report their itching assessments.

Note: Improved or no itching is an itching score reduction from baseline greater than or equal to 1 point on the scale or itching score of 0 at both baseline and post-baseline.

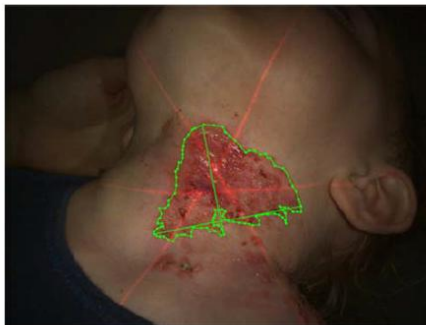
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Representative Before and After Pictures with SD-101-6.0 Simplex

Female EB Simplex Patient: 2 years old

2-year-old neck chronic wound
baseline



Wound treated with SD-101-6.0 and
completely closed within 1 month



Female EB Simplex Patient: 2 month old

2-month-old left foot chronic wound
baseline



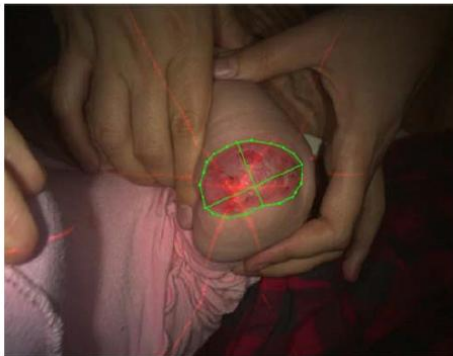
Wound treated with SD-101-6.0
and completely closed



Representative Before and After Pictures with SD-101-6.0 Recessive Dystrophic

Female RDEB Patient: 11 months old

11-month-old left elbow chronic wound
baseline



Wound treated with SD-101-6.0
and completely closed



Male RDEB Patient: 6 months old

6-month-old right buttock chronic wound
baseline



Wound treated with SD-101-6.0
and completely closed within 2 weeks



Representative Before and After Pictures with SD-101-6.0 Junctional

Male Junctional Patient: 4 years old

4-year-old lower right leg chronic wound
baseline



Wound treated with SD-101-6.0
and completely closed within 2 weeks



Male Junctional Patient: 25 years old

25-year-old lower left leg chronic wound
baseline



Wound treated with SD-101-6.0
and completely closed within 1 month



Excellent Safety Profile for Phase 3 and Phase 3 Open Label Extension Study with Zorblisa™ (Studies SD-005 and SD-006)

SD-005 Phase 3 Study

- The proportion of patients with TEAE skin infections was **statistically significantly lower (48% reduction) in the 6% Zorblisa^R group versus the placebo group (18.3 versus 33.3%, P=0.026)**
- Treatment-emergent adverse events (TEAE) similar across treatment groups, including placebo lotion
- One death in the placebo group and none in the Zorblisa™ group
- The incidence of TEAE serious adverse events were lower in the Zorblisa™ group versus the placebo group (4.9% versus 9.2% respectively)

SD-006 Open Label Extension Study

- **152 of 155 patients (98%) of patients completing Study SD-005 enrolled in the open label extension study (SD-006)**
 - Majority of patients completed 12 months of treatment prior to termination of study
 - Long term safety treatment with Zorblisa^R in subjects with Simplex, Junctional and Recessive Dystrophic EB was considered safe and well tolerated

Summary of Zorblisa™ Clinical Development Program

Two Placebo Controlled Clinical Trials (SD-003 and SD-005) and 2 Open Label Extension Studies (SD-004 and SD-006)

- Total of 217 EB patients (Simplex, Dystrophic and Junctional) treated with 6% Zorblisa™
- Data from the Phase 2b (SD-003) and Phase 3 (SD-005) studies were similar in terms of efficacy and safety
 - Locally delivered topical whole body therapy *without systemic absorption*
 - Daily whole skin surface administration of SD-101-6.0 was well tolerated
- 97% of patients completing participation in either SD-003 (Phase 2b) or SD-005 (Phase 3) studies continued on open label therapy
- Zorblisa™ is the only local whole body treatment to demonstrate clinically relevant safety and efficacy across all EB subtypes

Clearly Defined Registration Paths in US, EU, and Japan



- Agreements with FDA
 - Single registration trial
 - Approved primary endpoint
 - Preclinical, CMC requirements defined and completed
 - Treatment across all subtypes, ages 1 month and older



- Clinical program to support registration in Europe
 - PDCO agreed Pediatric Investigation Plan (PIP) – identical to US development plan
 - CMC and non-clinical programs agreed

\$2+B Commercial opportunity in Multiple Markets

No current treatment



Compelling efficacy data,
rare pediatric and orphan
designations provide
rationale for access



Large commercial
opportunity

- Only therapy for EB targeting all subtypes
- Only therapy for pediatric and adult patients
- Current palliative treatments are costly and time-consuming

- Compelling Phase 2a, Phase 2b, and Phase 3 efficacy data
- Orphan drug pricing
- First effective treatment for EB across all subtypes – chronic therapy
- Long-term safety established

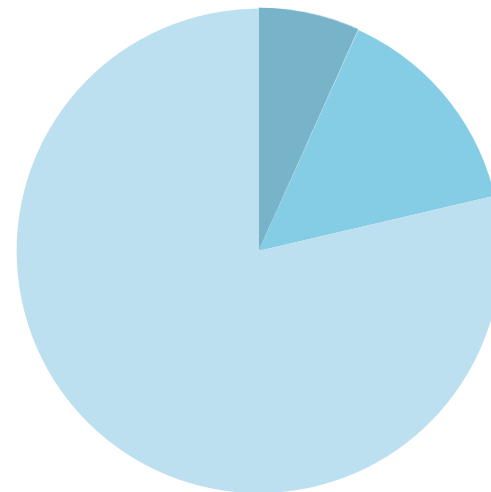
- **First EB treatment to market to treat whole body targeting of all EB subtypes**
- Specialty market of consolidated centers of EB excellence
- Specialty sales force of no more than 25 sales representatives

Prevalence of EB

■ US 20,000–40,000

■ EU 50,000–80,000

■ ROW 300,000–400,000



Paradigm will Receive a FDA Priority Review Voucher at Approval

- **Paradigm's development program for Zorblisa™ for the treatment of EB will qualify for an FDA rare pediatric priority review voucher (PRV)**
 - FDA identifies EB as rare, pediatric disease
 - Voucher is fully transferable and can be sold
 - Voucher entitles PRV holder to have a priority review of their NDA, shortening the FDA review period to 6 months from the standard 12 month review
 - Expedites earlier market entry of therapeutic
- **Rare Pediatric Disease priority review voucher recent sales between \$100-150M (highest sale \$350M)**

Investment Highlights

- **Short timeline to commercial approval – estimated less than 1.5 years in US, with receipt of Priority Review Voucher (estimated value recently between \$100-150M, with highest sale of \$350M)**
- **High gross margin with very low cost of goods (COGS) while being reasonably priced for payers and still a \$2 Billion+ commercial market**
- **Treatment of all subtypes of EB is a significant unmet medical need**
 - Significant US, EU, Japan, and ROW prevalence with no approved therapeutics
- **Zorblisa™ is the first and only whole body treatment to demonstrate safety and efficacy targeting all EB subtypes in pediatrics and adults**
 - **Clinically significant results in Phase 2a, 2b and Phase 3 trials (217 EB patients)** with no adverse events of concern
 - **Locally** delivered whole body topical therapy across skin *without systemic absorption*
 - **Only therapy** to treat all EB subtypes with demonstrated reduction of whole body wounds and lesions
- **Potential for significant profitability drives valuation**
 - Orphan drug market pricing, data exclusivity periods long
 - Low cost of goods (COGS) – less than 5%
 - Ability to commercialize with a targeted, cost-efficient sales force

New Manufacturing in place to produce commercial supplies to support global distribution