Improving Lives of People with Rare Diseases

Paradigm Therapeutics
Partner in Rare Diseases

Our Mission

Paradigm Therapeutics is dedicated to the development of Zorblisa™, which is an innovative 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

Singular focus on a rare diseases with significant medical need

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

Zorblisa™ (allantoin)

Demonstrated robust efficacy and safety

Convenient once daily, topical administration

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

"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

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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

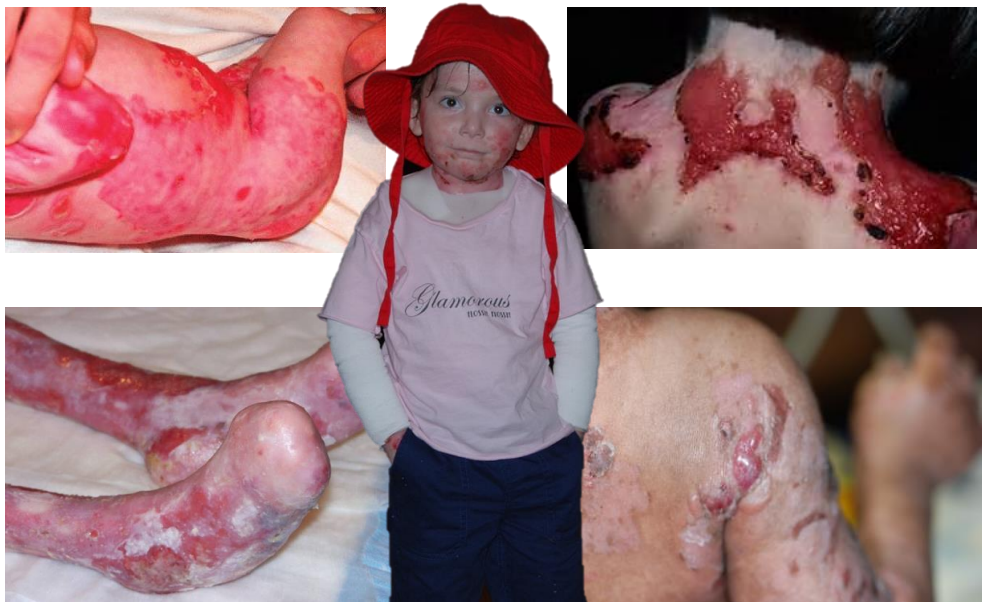
Highly experienced Clinical Operations Executive with 29+ years in the field of clinical research, including senior roles at major CRO and pharmaceutical companies

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 of[1]"



[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)

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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."

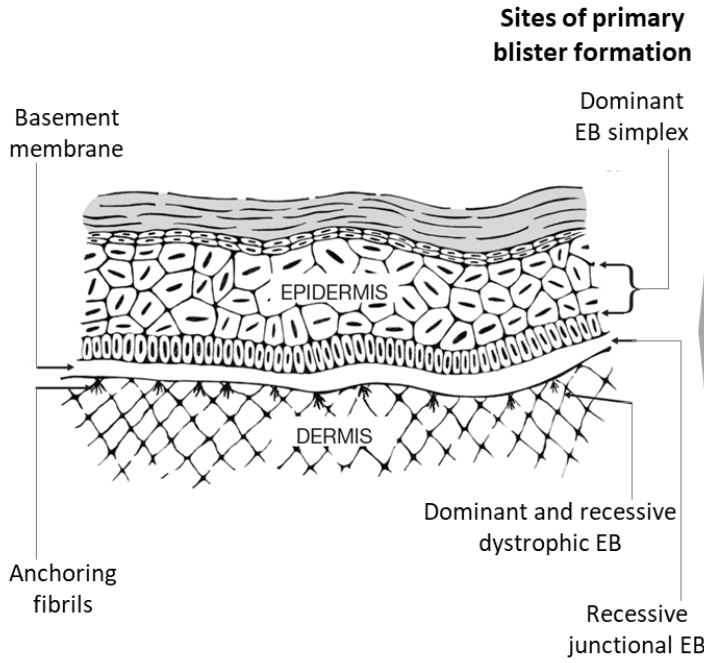
- **EU: Est. 50,000 to 80,000 current cases**
  - Gabriella Pohln-Gubo (5th International Conference on rare diseases-Krakow 2010)
  - Prevalence estimates in Northern Europe
    - Northern Ireland ~ 44/M (Covello et al. J INV DERM, 1998)
    - Scotland ~ 49/M (Horn et al. BRIT J DERM, 2008)

- **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)

- **<u>Worldwide prevalence estimated at 500,000 patients</u>**

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

Skin structure



Source: Adapted from DEBRA America

EB subtypes

Subtypes	Symptoms	Frequency	Mortality risk
Simplex	➢ Blistering on hands and feet (localized) ➢ Blistering all over body (generalized)	~75%	
Dystrophic	➢ Contraction of joints ➢ Fusion of fingers and toes ➢ Contraction of mouth membranes ➢ Narrowing of esophagus ➢ Possibility of skin cancer	~20%	
Junctional	➢ 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%	

**Kindler EB is a very rare 4th type of EB with about 250 affected individuals reported worldwide*

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

- **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 Only 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

Zorblisa™ is in Development as 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**
  - Demonstrated efficacy and excellent safety in Phase 2a, Phase 2b, and Phase 3 trials
  - Zorblisa™ has 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
- **FDA-awarded breakthrough therapy designation providing a well-defined, risk-mitigated regulatory pathway**
  - Awarded based on Phase 2 demonstration of significant clinical benefit in closure of wounds and reduction in body surface area (BSA) of blisters and lesions

Comparison of Zorblisa™ versus Late-Stage EB Programs in Development or Approved
Key Differentiating Characteristics

	Zorblisa™*	Amryt**	Castle Creek	Krystal***	Abeona
Patient Population	**Simplex, Junctional and Dystrophic**	Recessive Dystrophic only	Recessive Dystrophic only	Recessive Dystrophic only	Recessive Dystrophic only
Treatment Area	**Whole body**	Single wound	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 – chronic therapy	Topical	Intradermal Injection	Topical	Transplantation

* Benefits specifically for Zorblisa™ compared to competitors in **"bold"**

**FDA did not approve
*** Recently approved in US to treat only a single wound – yearly price in excess of $600K

Summary of Zorblisa™ Clinical Phase 2 and 3 Results to Date Simplex, Junctional and Dystrophic EB Patients

Summary of Zorblisa^{R} Clinical Development Program

- **Two Placebo Controlled Clinical Trials (Phase 2b and 3) with Similar Efficacy and Safety Results**
  - **Total of 217 EB patients (Simplex, Dystrophic and Junctional) treated with 6% Zorblisa^{R}**
  - **Locally** delivered topical whole body therapy *without systemic absorption*
- **Zorblisa^{R} is in development as the only local whole body treatment to evaluate clinically relevant safety and efficacy across all EB subtypes**
  - **Rapid Target Wound Closure**
    - Proportion of patients with complete closure higher than placebo beginning at first visit (week 2) and continuing throughout trial in both studies
    - Median time to complete wound healing much faster in Zorblisa-treated patients versus patients on placebo
  - **Rapid Reduction in Whole Body Coverage in Lesional Skin and Wounds**
    - Phase 2 - Reduction in whole body coverage in lesional skin (wounds and blisters) 28% in Zorblisa-treated patients versus 5.75% reduction in placebo patients by month 3
    - Phase 3 - Reduction in whole body wound burden in Zorblisa-treated patients versus placebo patients by week 2 and continuing throughout study, in patients will all levels of wound burden at baseline
  - **Reduction in Skin Infection**
    - **Phase 3 - The proportion of patients with skin infections was statistically significantly lower in the Zorblisa^{TM} group versus the placebo group (18.3 versus 33.3%, P=0.026))**
    - **Phase 2 - Skin infections reported were higher in the placebo group (5.9%) compared to the Zorblisa-treated group (none reported)**

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

Unmet Patient Need in Multiple Markets

No current treatment

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

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Compelling efficacy data and breakthrough designation provide rationale for access

- Compelling Phase 2a, Phase 2b, and Phase 3 efficacy data
- Orphan drug pricing
- In development as an effective treatment for EB across all subtypes – chronic therapy
- Long-term safety has been conducted

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Large commercial opportunity

- **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