Krystal

Medicines for Skin Diseases and Conditions –
A Gene Therapy Company

GEM-2 KB103 Phase 2 Clinical Study Update
June 24, 2019

Forward-Looking Statements

This webcast and the slides accompanying it contain data from Krystal's phase 1/2 trial evaluating KB-103 in patients suffering from Dystrophic epidermolysis bullosa, or DEB. Statements made in the webcast and slides may contain "forward-looking statements" regarding matters that are not historical facts, including statements relating to the Company's clinical trials and product development pipeline. There can be no assurance that the data contained in these results will be replicated in additional patients enrolled in this or any future trial, or that these results will prove clinically meaningful in the development of KB103 as a potential drug. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Words such as "anticipates," "plans," "expects," "intends," "will," "potential," "hope" and similar expressions are intended to identify forward-looking statements. These forward-looking statements are based upon current expectations of the Company and involve assumptions that may never materialize or may prove to be incorrect. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties. Detailed information regarding factors that may cause actual results to differ materially from the results expressed or implied by statements in this press release relating to the Company may be found in the Company's periodic filings with the Securities and Exchange Commission..

Dystrophic Epidermolysis Bullosa (DEB)

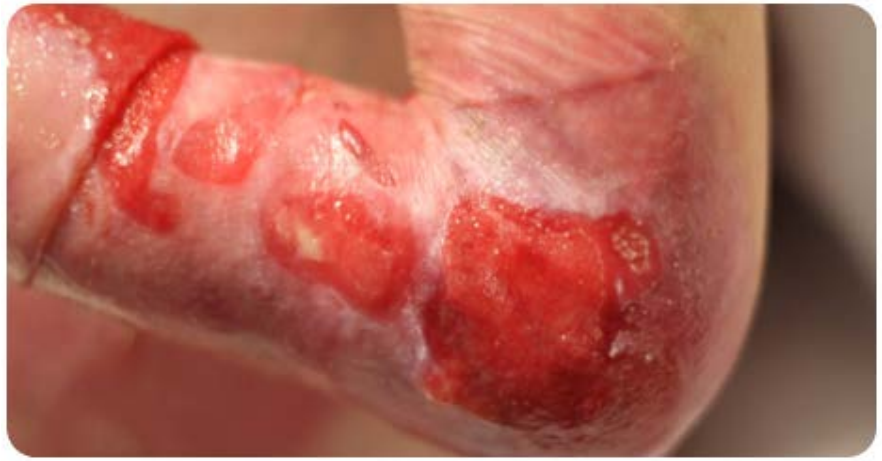
"Butterfly Children" is used to describe young DEB patients because their skin is as fragile as a butterfly's wings

Dystrophic Epidermolysis Bullosa

A rare, genetic connective tissue disease that causes skin to tear or blister from minor contact

Caused by a mutation in the COL7A1 gene that codes for the COL7 protein

Without COL7 the epidermis does not anchor to the dermis



Epidemiology

Prevalence: ~10,000 people are affected by DEB worldwide[1,2]

Incidence: The incidence of DEB is 6.5 per million births in the US[2]

Current Standard of Care

There are no approved treatments for DEB

Existing therapies limited to expensive and time-consuming palliative treatments

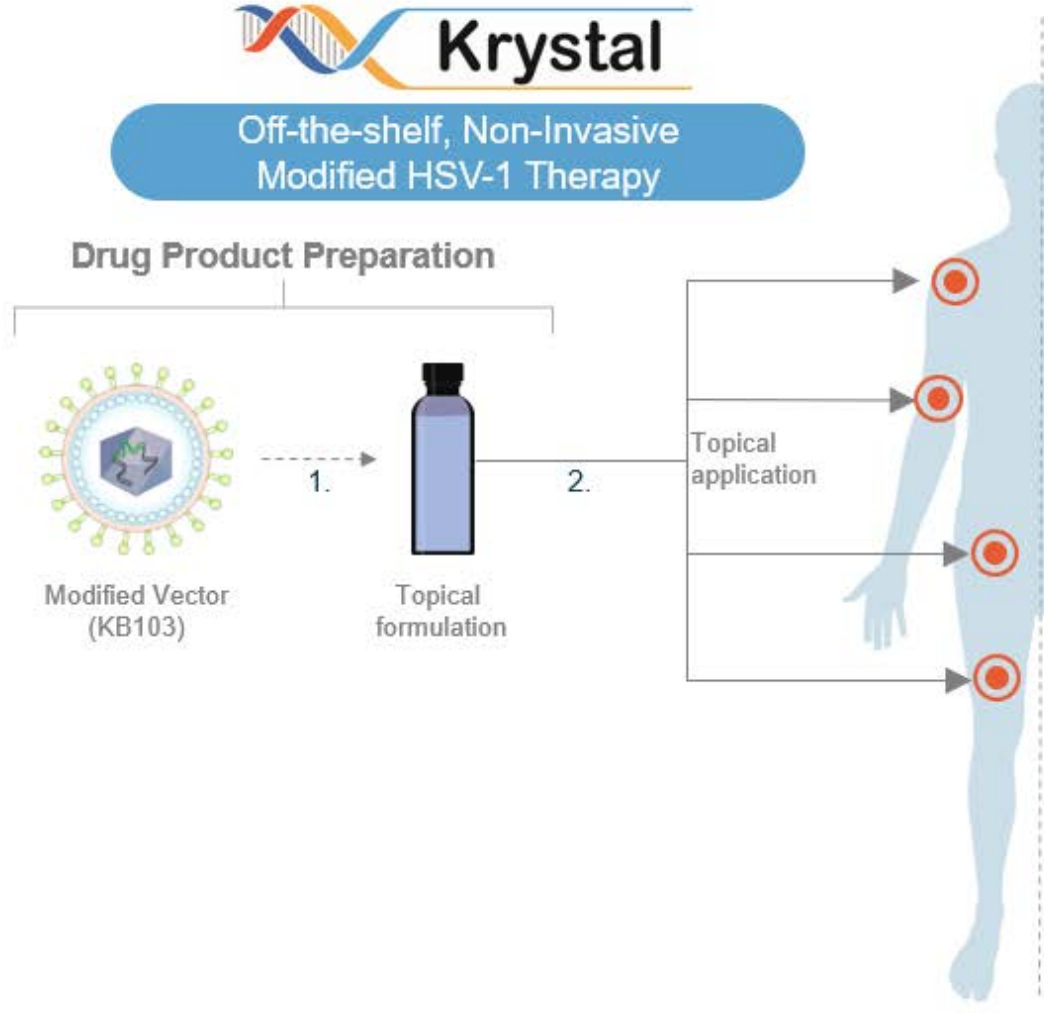
Palliative treatments cost $200k – $400k annually[3,4]

1. DEBRA International, http://www.debra-international.org/epidermolysis-bullosa/causes-and-subtypes.html; http://www.debra-international.org/what-is-eb/causes-and-subtypes/deb.html
2. Pfendner EG, Lucky AW. Dystrophic Epidermolysis Bullosa. 2006 Aug 21 [Updated 2015 Feb 26]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet].
3. Rashidghamat E., Mellerio J.E., Management of chronic wounds in patients with dystrophic epidermolysis bullosa: challenges and solutions, Chronic Wound Care Management and Research Volume 2017:4, 45-54
4. GENEGRAFT Report Summary. (2015, February 16). Retrieved December 13, 2016, from http://cordis.europa.eu/result/rcn/156078_en.html

Disease burden

- Clinical endpoints
  - Time to wound closure (days)
  - Percentage of wound closure (area %)
  - Duration of wound closure (days)
- Evidence of mechanistic endpoints
  - Presence of NC1 and NC2 domains demonstrating production of functional COL7
  - NC1 and NC2 staining of anchoring fibrils
- Chronic wounds vs Recurring wounds
  - Chronic wounds tend to stay open (~ > 12 weeks)
  - Recurring wounds tend to close and open frequently due to absence of anchoring fibrils
  - Recurring wounds more prone to squamous carcinoma

KB103: Simple, Painless and Easy to Administer



Benefits of Krystal's approach to treat DEB

- "Off-the-Shelf" product ready for use in multiple patients
- Manufacturing and supply chain costs are lower – direct ship to local site
- Therapy can be administered by any dermatologist, primary care physician, care giver, nurse
- No hospitalization needed
- Does not require expensive, invasive, and time-consuming procedures. sophisticated medical teams or travel to specialty centers

KB103 Phase 1/2 Status update

- Phase 1 (GEM-1) update
  - Krystal announced interim data on 4 wounds (up to 10 cm^2 in area) in 2 patients (2 active, 2 placebo) in October, 2018
    - 100% wound closure (by area) observed in both wounds treated with KB103
    - Average time to wound closure was 12 days (median 12 days)
    - The duration of wound closure on two patients following 100% wound closure as of the last follow up was 184 days (6.6 months) and 174 days (6.2 months) respectively

- Phase 2 (GEM-2) study is the focus of current presentation:
    - Four additional new patients were dosed in second half of December 2018
    - Individual analysis of GEM-2 and combined analysis of GEM-1 and GEM-2

KB103 Phase 2 Study Results

GEM-2: Phase 2 Trial Design

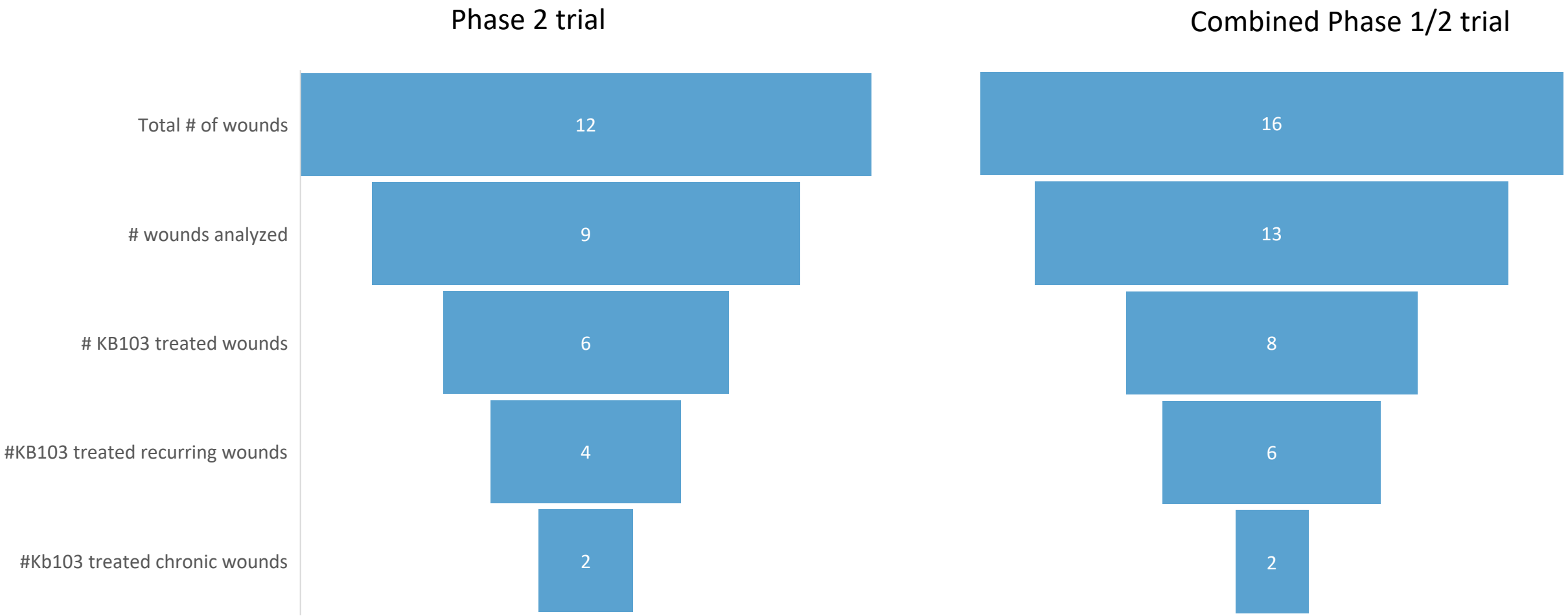
Four patients enrolled in December, 2018. Principal Investigator: Dr. Peter Marinkovich, Stanford University

- **Key objectives**: Demonstrate efficacy and safety of KB103
  - **Primary Clinical Objectives**: Safety and Wound healing (time to wound closure, % area of wound closure, duration of wound closure)
  - **Secondary Mechanistic Objectives**: Expression of COL7, evidence of anchoring fibrils.

- **Trial Design**:

  - Randomized, placebo controlled study; 4 patients enrolled in study – 2 adult 2 pediatric
  - 3 wounds treated topically in each patient: 1 placebo, 2 active
  - Total number of wounds treated in Phase 2 study = 12 (3 wounds per patient * 4 patients)
  - Initial front loaded dosing for 5 days (3e8 pfu/day)
  - Biopsies were based on PI discretion during site visits.
  - Biopsied wounds were dosed one administration of 3e8 at site of biopsy, following a biopsy
  - Each patient is on-study for approximately six months; three months of on-site visits followed by a 3-month at-home imaging period

Wound characterization in Phase 2 and combined trial



One patient in Phase 2 trial dropped out of the study after 30 days due to an inability to travel resulting in analysis on remaining three patients (9 wounds)
Chronic wounds remain open for greater than or equal to 12 weeks while recurring wounds heal but easily open

GEM-2: KB103 Safety Update in Wounds

KB103 continues to be well tolerated to date following first and repeat dose

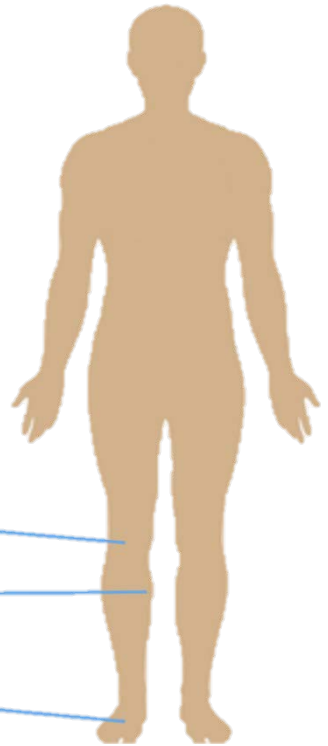
- No treatment-related adverse events (serious or otherwise) were reported.
- No immune response or blistering observed around the sites of administration following first and repeat dose.
- Blood and urine samples collected throughout the study revealed:
  - No viral shedding
  - No adverse events associated with routine labs (chemistry and hematology)
  - No antibodies to COL7 was detected

KB103 Study Results

(Wound Healing)

Gem-2 Study: Patient 1 (Age 13)

Wound	Type	Treatment	Baseline area in cm^2	Days to 100% wound closure	% Area Closure			Duration of Closure at Day 90
					Day 30	Day 60	Day 90	
2	Recurring	KB103	15.6	22	100%	100%	100%	68
3	Recurring	KB103	14.9	10	100%	100%	100%	80
1	Recurring	Placebo	3.6	n/a	72%	Fully open	Fully open	n/a



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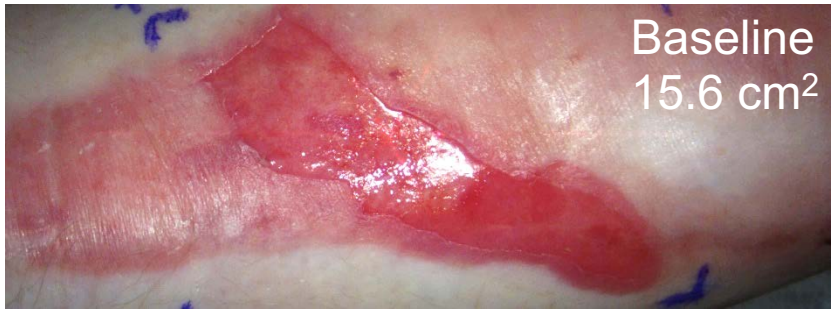
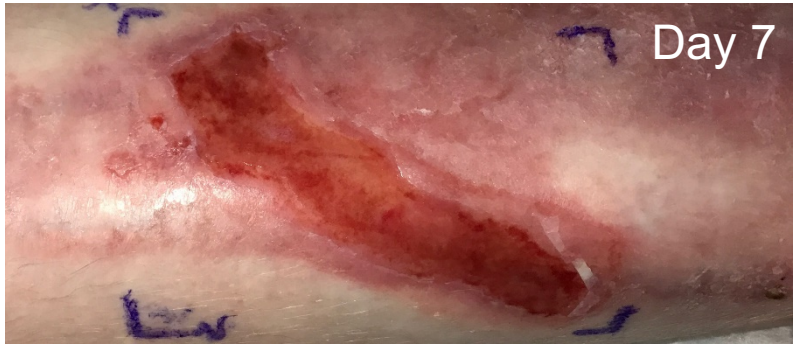
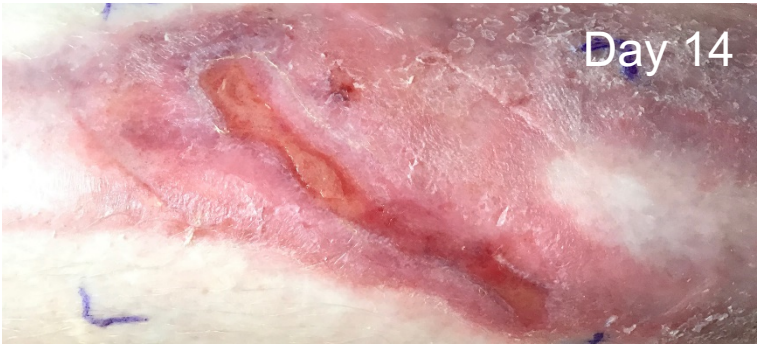
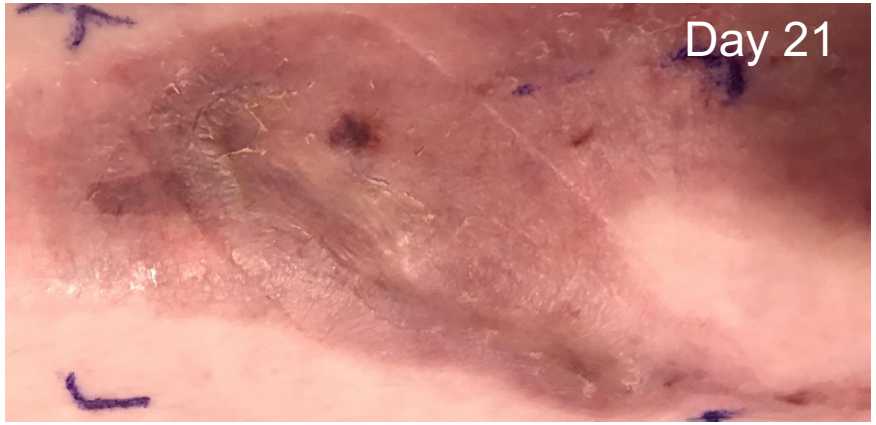
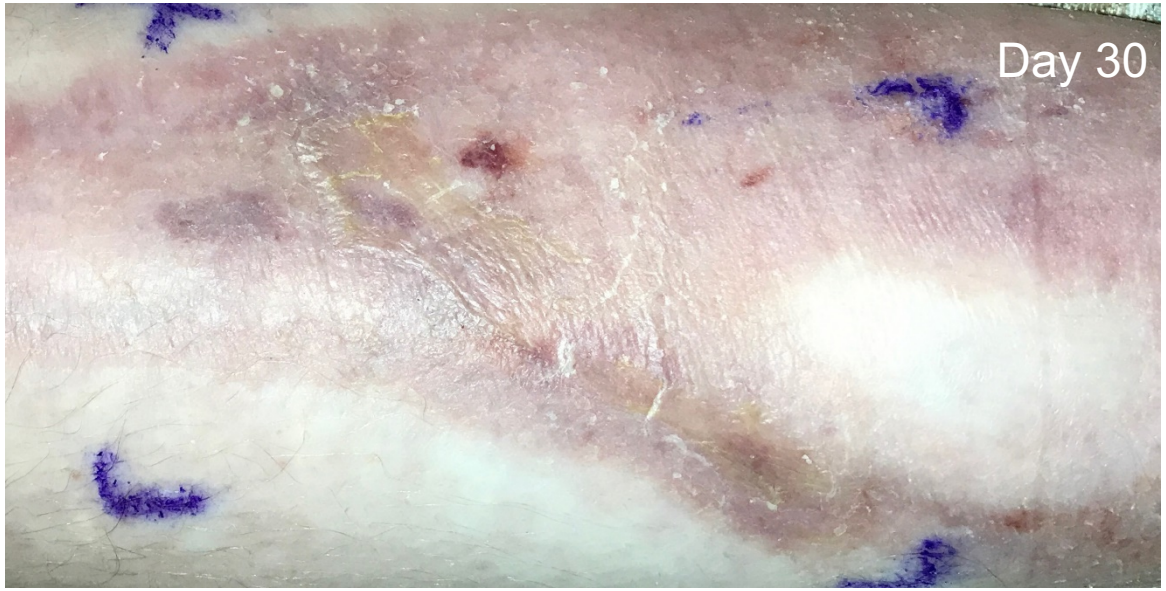
Wound Healing on Wound 2 in the first month











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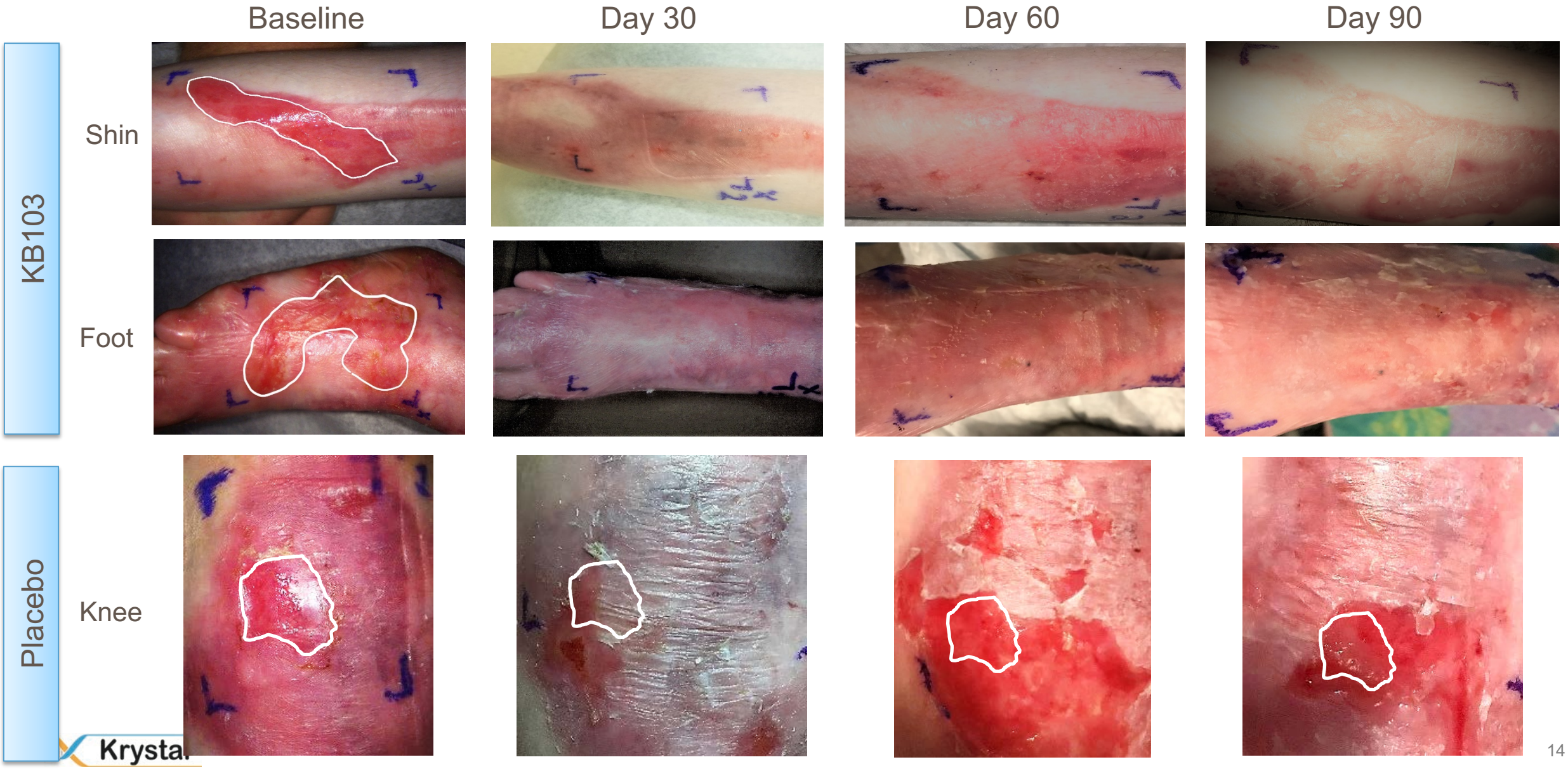
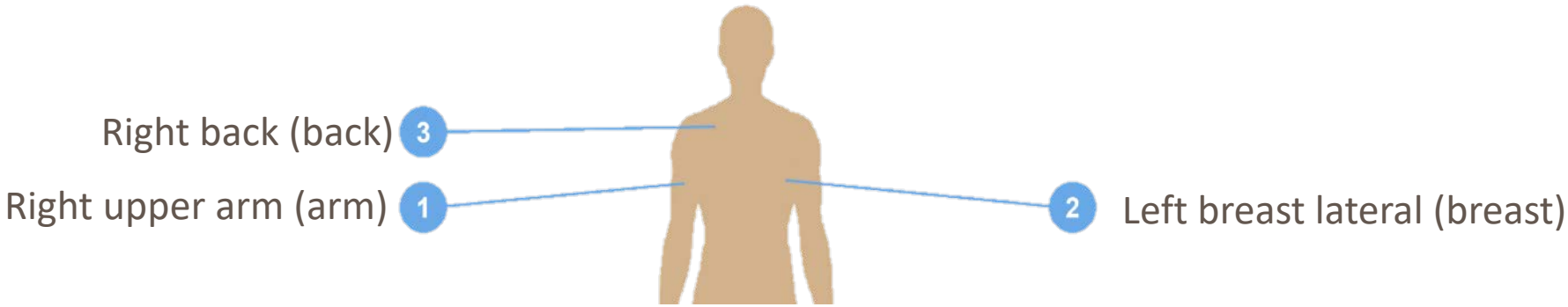
Gem-2 Study: Patient 1 (Age 13)



Gem-2 Study: Patient 2 (Age 14)



Wound#	Type	Treatment	Baseline area in cm^2	Days to 100% wound closure	% Area Closure			Duration of Closure at Day 90
					Day 30	Day 60	Day 90	
1	Chronic	KB103	9.7	41	88.7%	100%	95.9%	49
3	Recurring	KB103	15.2	24*	100%	100%	100%	66
2	Recurring	Placebo	6.2	n/a	10.6%	45%	Fully open	n/a

On wound 3, >90% of the wound had closed by Day 14

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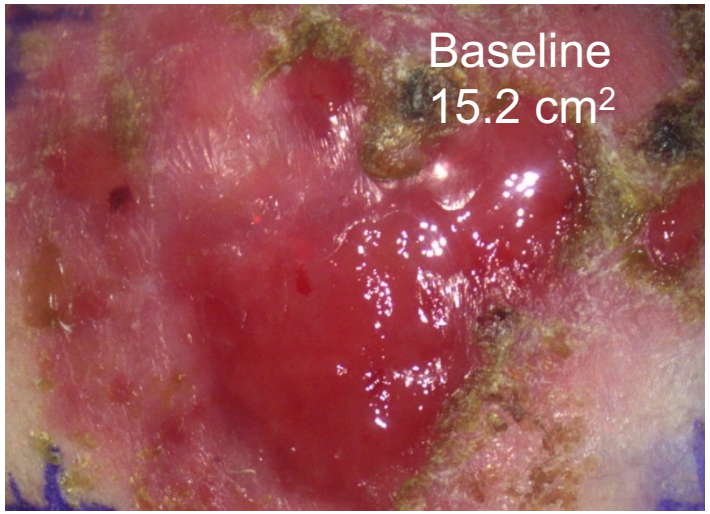
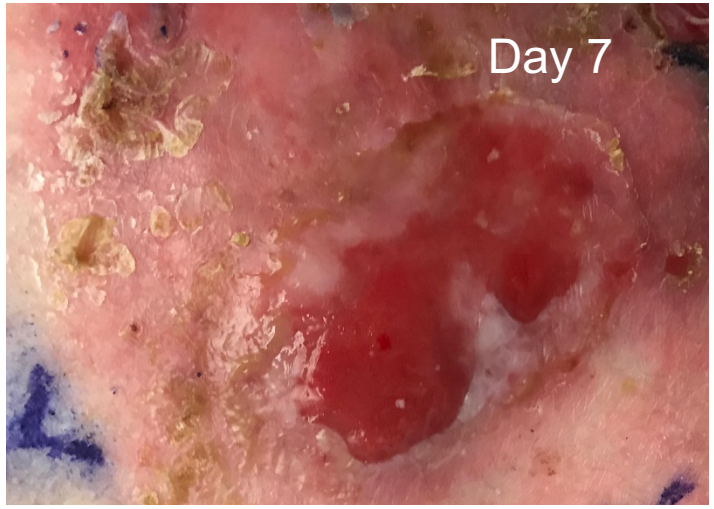
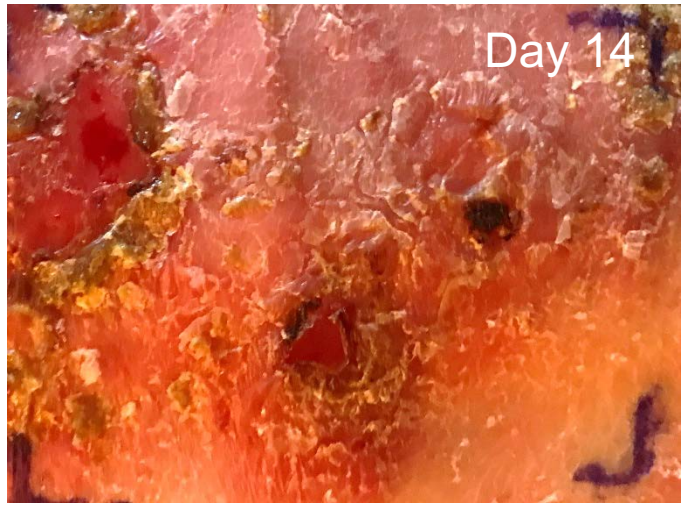
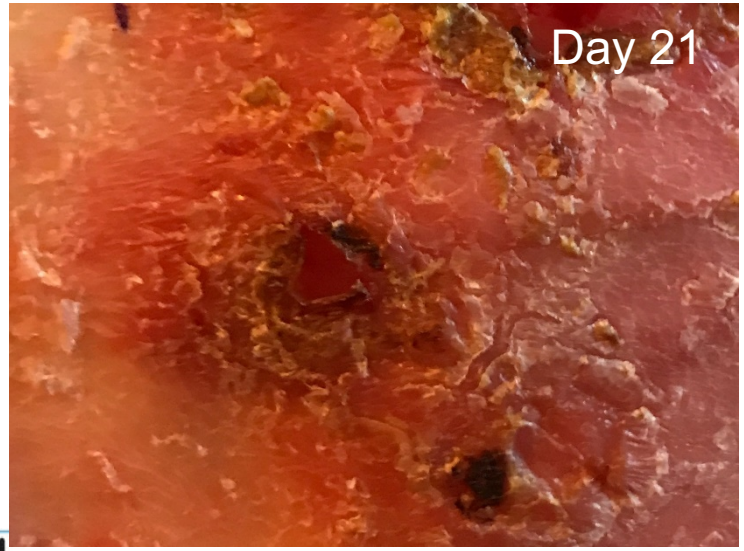
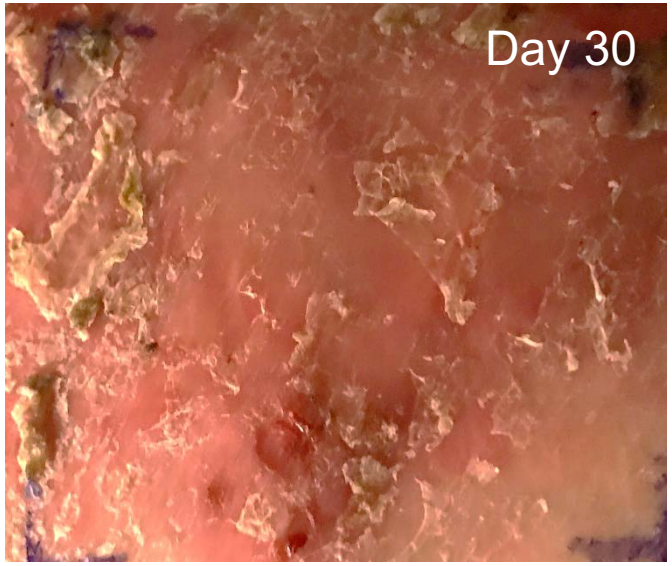
Wound Healing on Wound 3 in the first month



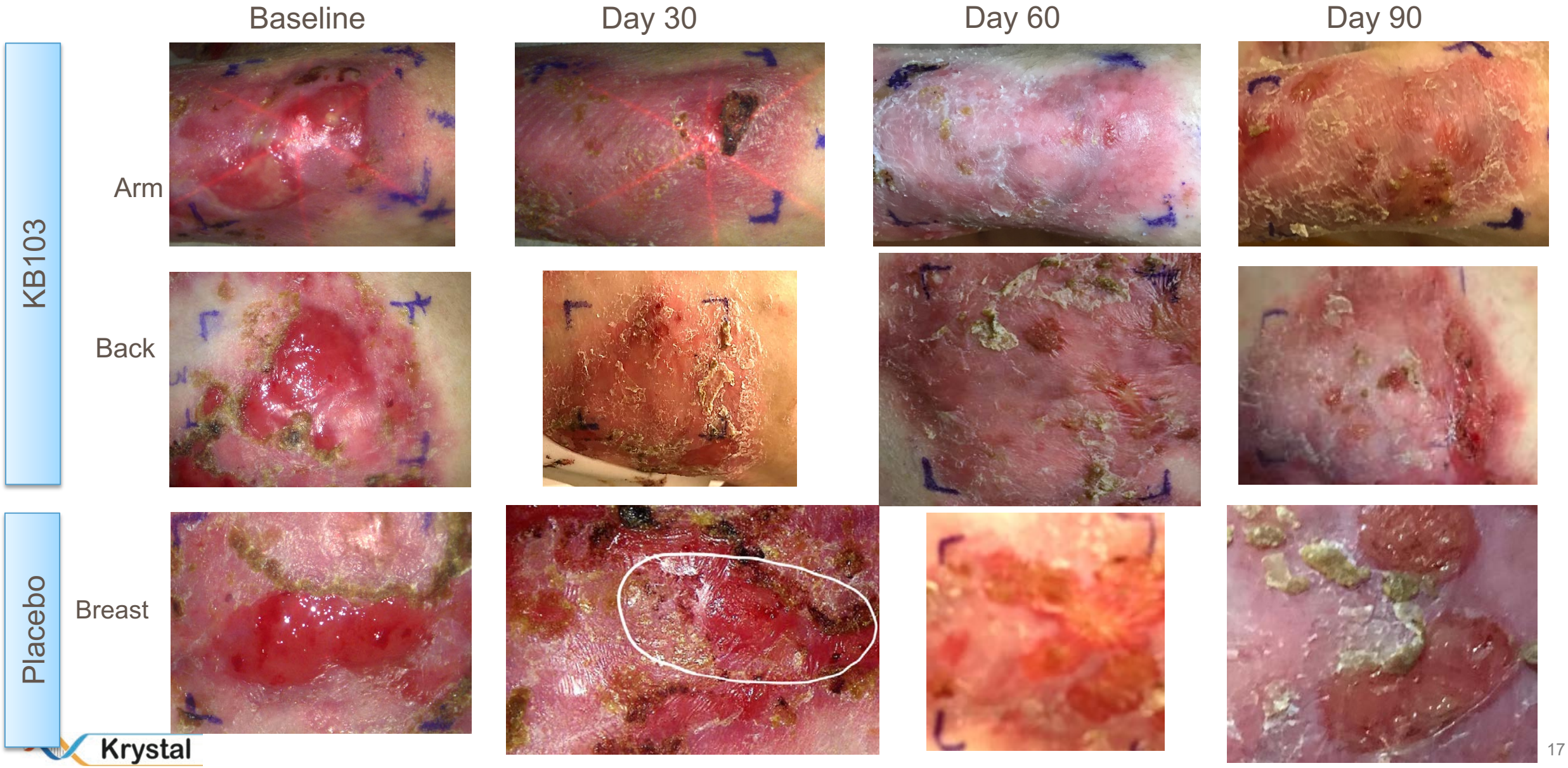






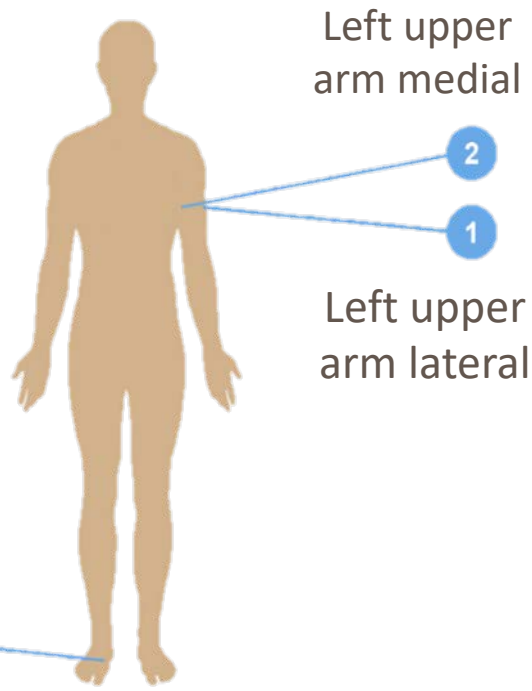


Gem-2 Study: Patient 2 (Age 14)

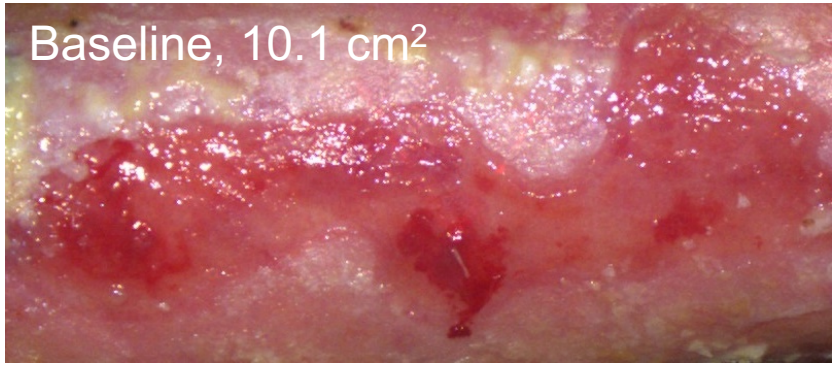


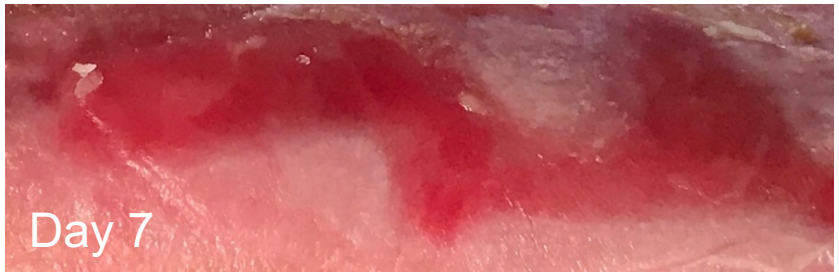
Gem-2 Study: Patient 3 (Age 22)

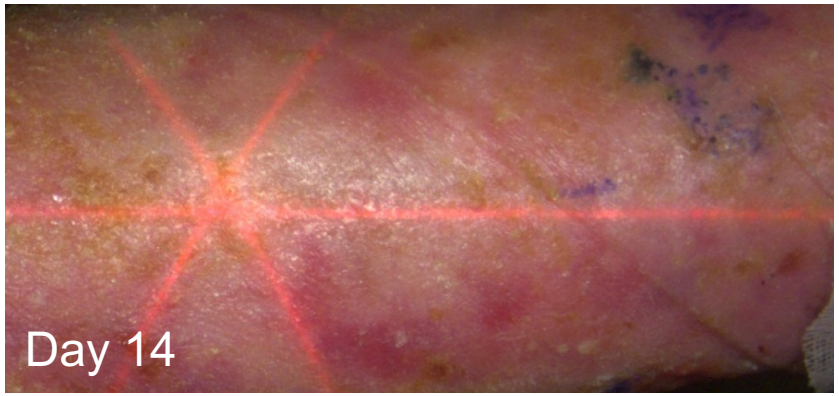
Wound	Type	Treatment	Baseline area in cm^2	Days to 100% wound closure	% Area Closure			Duration of Closure at Day 90
					Day 30	Day 60	Day 90	
1	Recurring	KB103	10.1	20	100%	100%	100%	70
3	Chronic	KB103	6.0	~42% closure on Day 90	35%	40%	41.7%	
2	Recurring	Placebo	3.1	n/a	9.7%	Fully open	Fully open	n/a

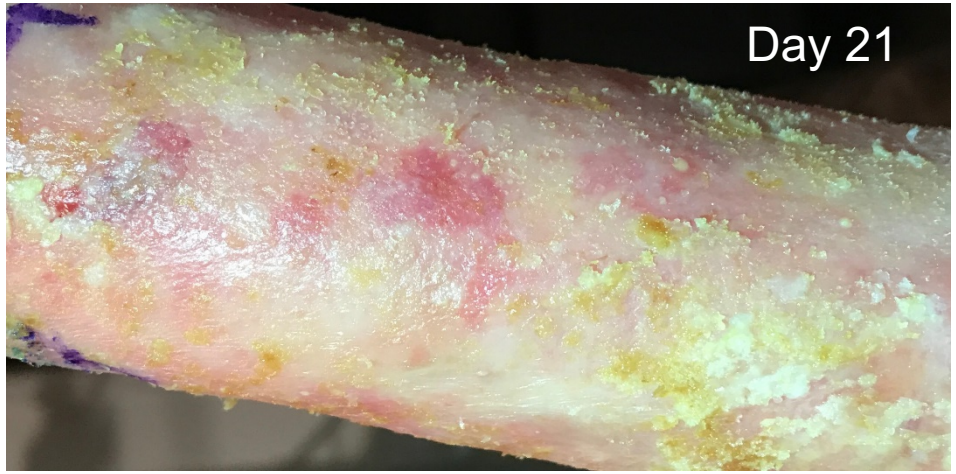


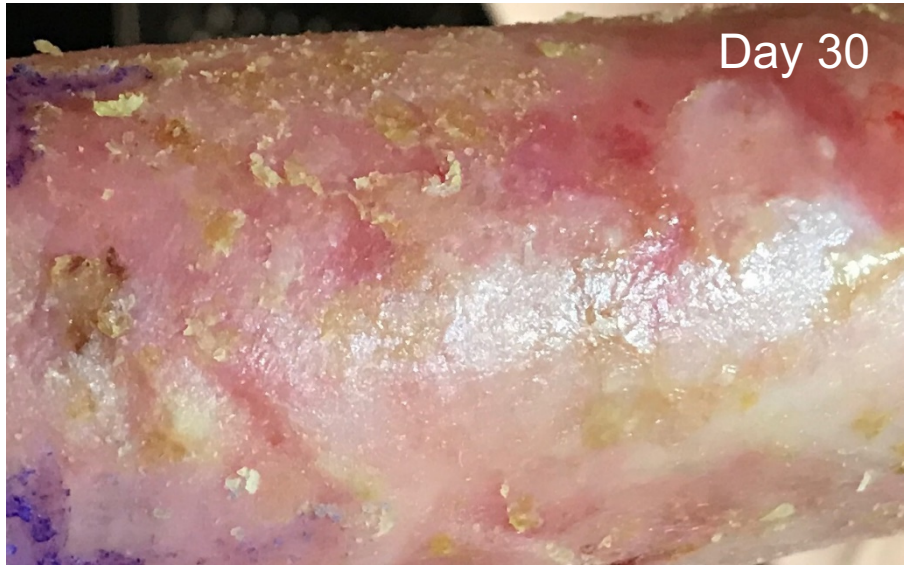
Wound Healing on Wound 1 in the first month (circle wound area)











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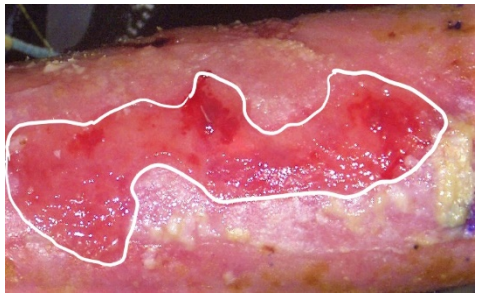
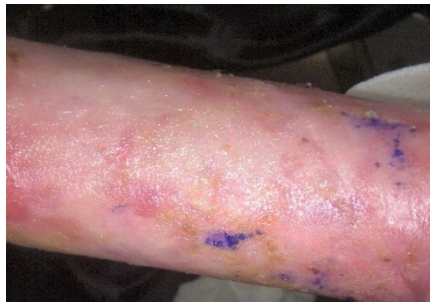
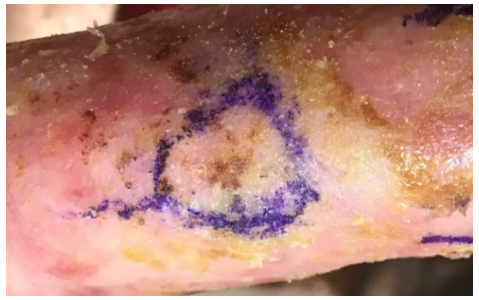
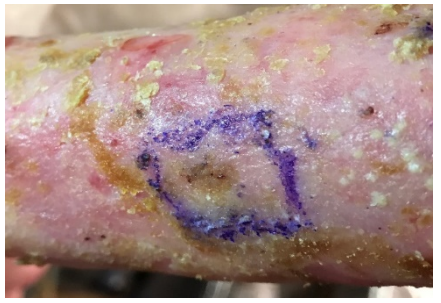
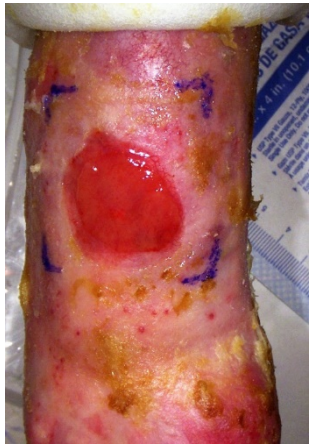
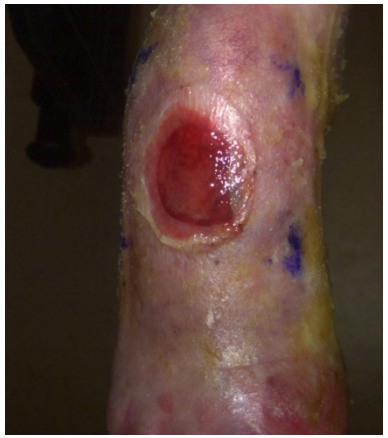
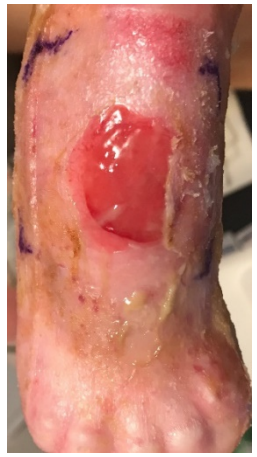
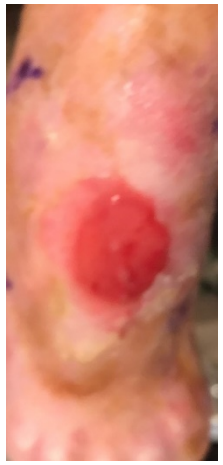
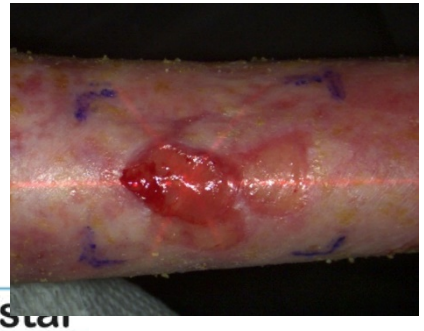
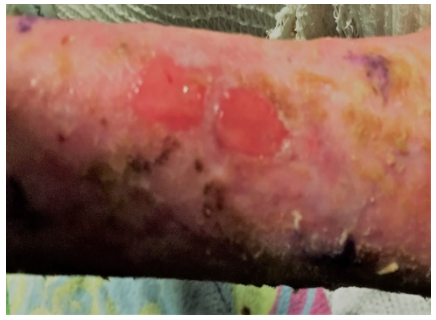
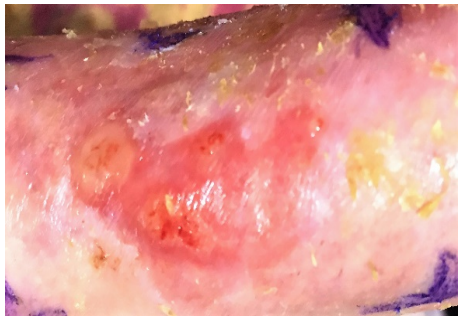
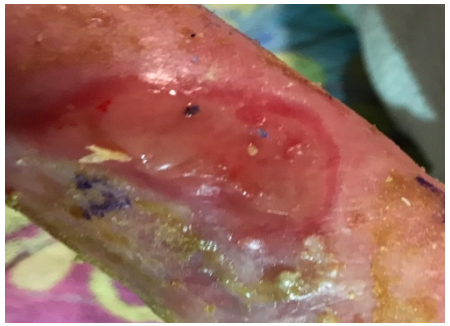
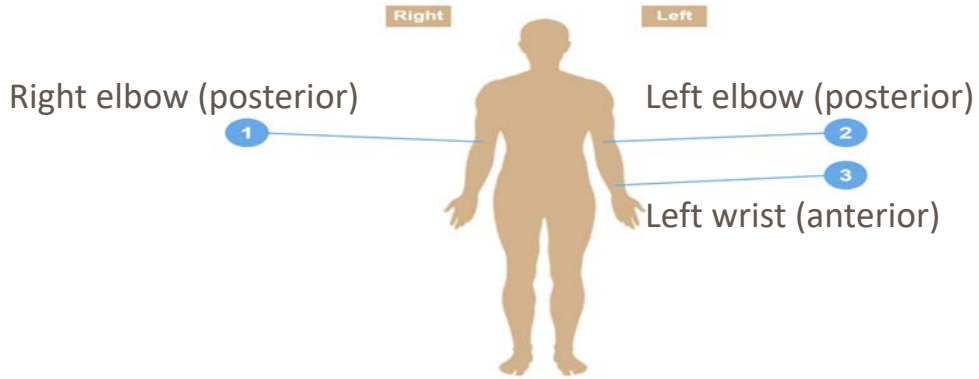
Gem-2 Study: Patient 3 (Age 22)

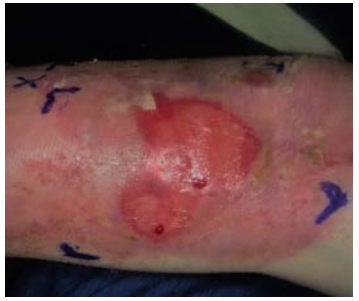
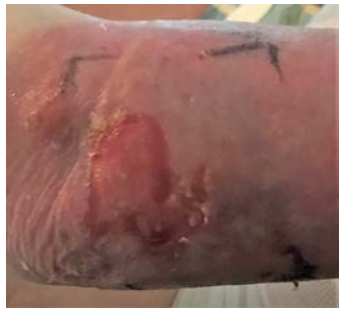
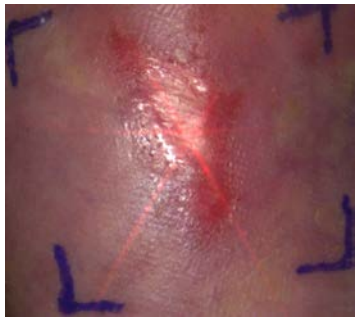
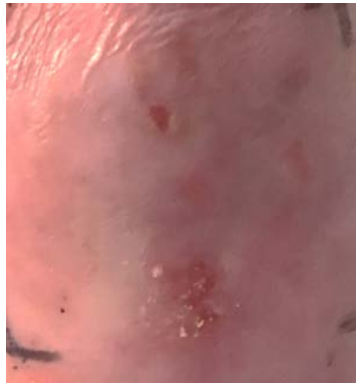
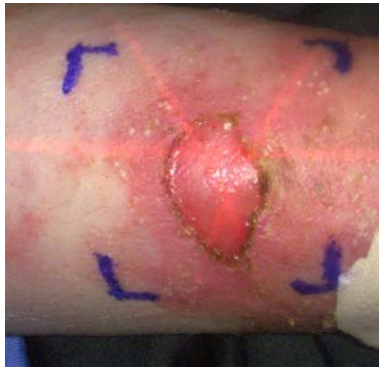
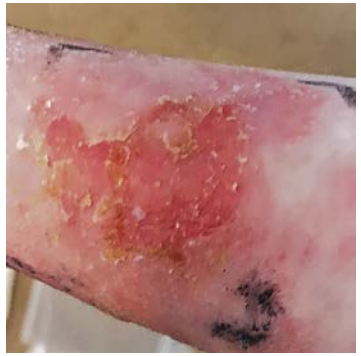
		Baseline	Day 30	Day 60	Day 90
KB103	Arm				
	Foot				
Placebo	Arm				

Gem-2 Study: Patient 4 (Age 19) – Dropped out of study after 30 days



Wound	Type	Treatment	Baseline area in cm^2	Days to Closure	% Area Closure			Duration of Closure at Day 90
					Day 30	Day 60	Day 90	
1	Chronic	KB103	12.5		60%			
2	Recurring	KB103	5.0	20 days	100%			
3	Recurring	Placebo	2.3	n/a	0%			

Gem-2 Study: Patient 4 (Age 19) – Dropped out of study at Day 30

		Baseline	Day 30
KB103	Right Elbow		
KB103	Left Elbow		
Placebo	Left Wrist		

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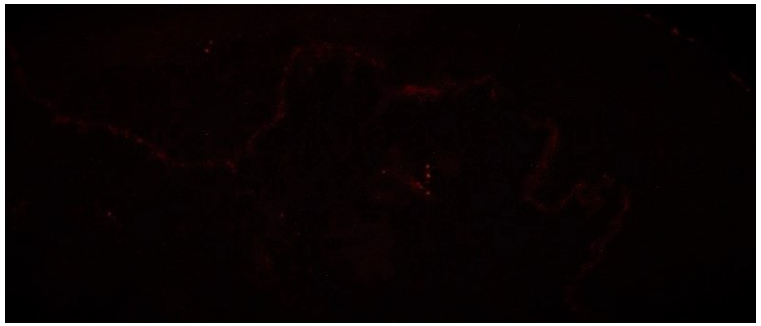
KB103 Study Results

(Mechanistic endpoints)

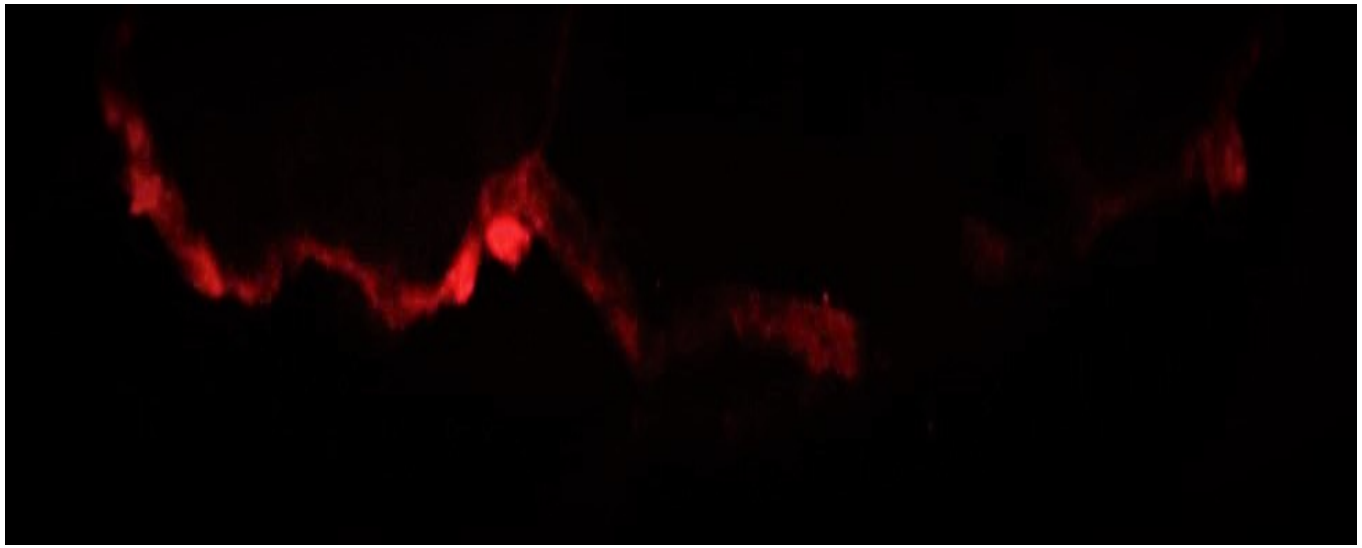
Functional COL7 expression in Patient 1

Presence of NC1 and NC2 domains demonstrating functional COL7 linearly deposited on basement membrane zone

Baseline

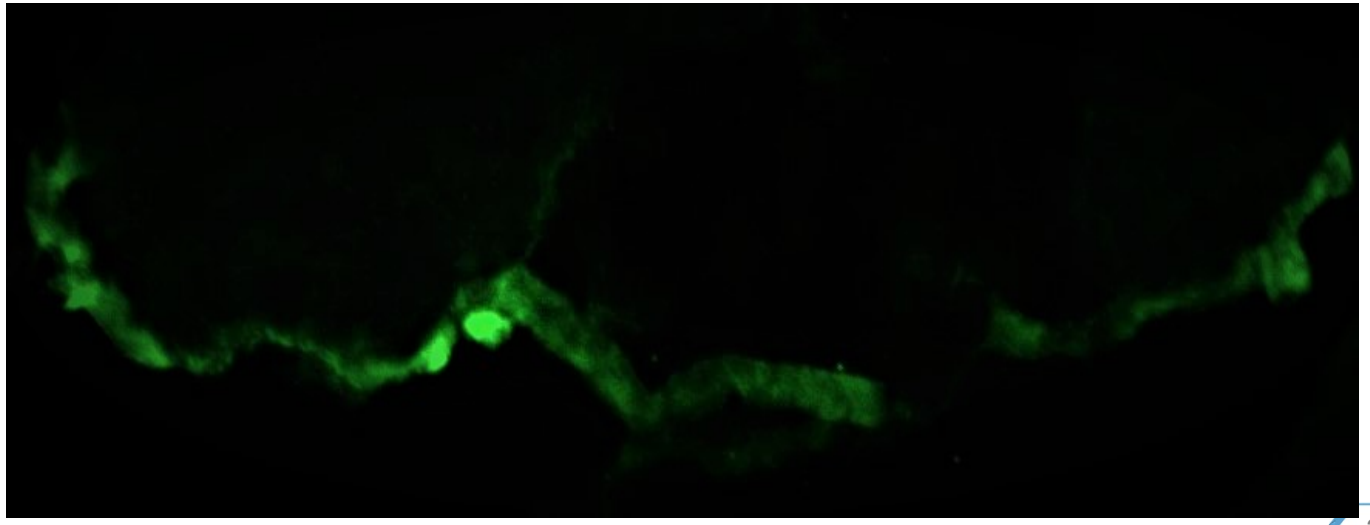


← NC1 -->



Baseline

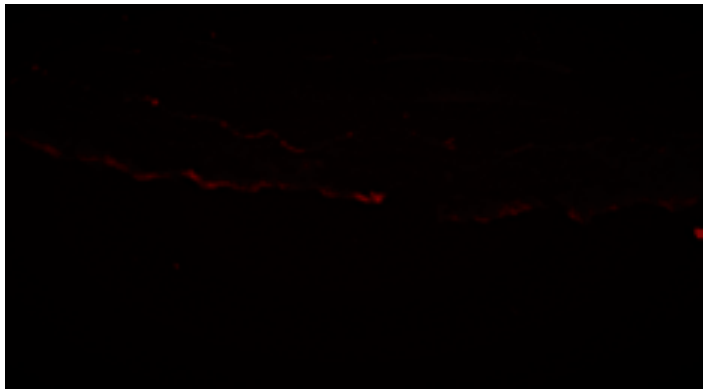
<-- NC2 -->



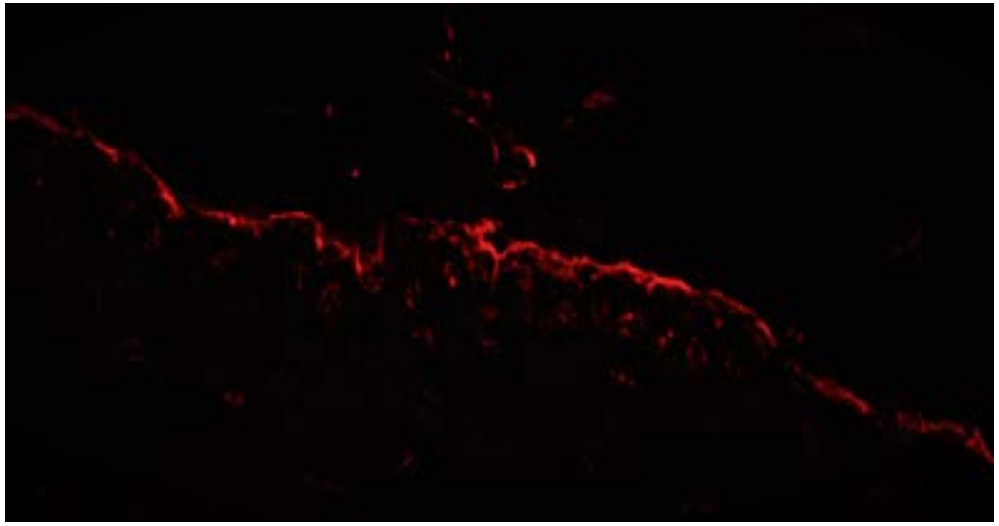
Functional COL7 expression in Patient 2

Presence of NC1 and NC2 domains demonstrating functional COL7 linearly deposited on basement membrane zone

Baseline

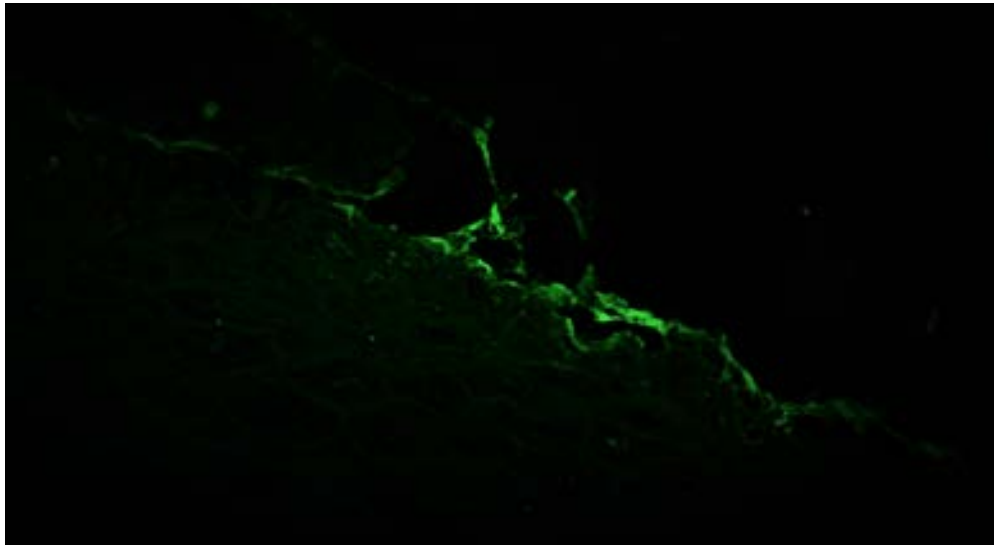


<- NC1 ->



Baseline

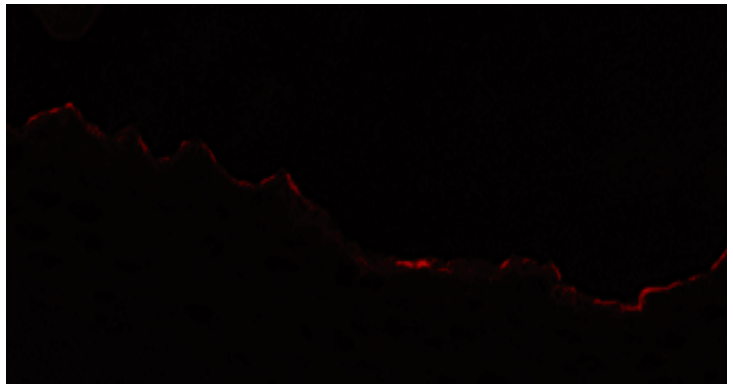
<- NC2 ->



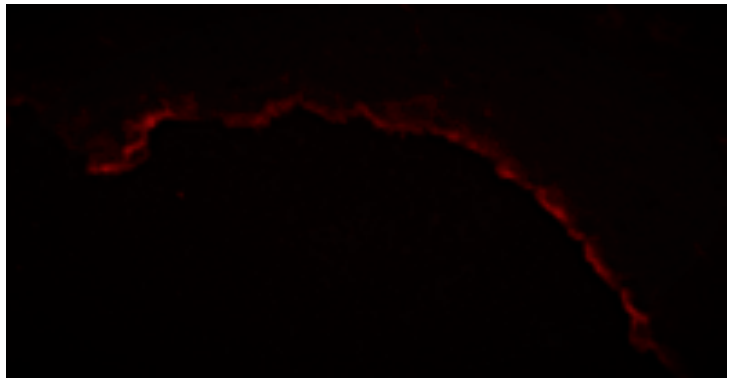
Functional COL7 expression in Patient 3

Presence of NC1 and NC2 domains demonstrating functional COL7 linearly deposited on basement membrane zone

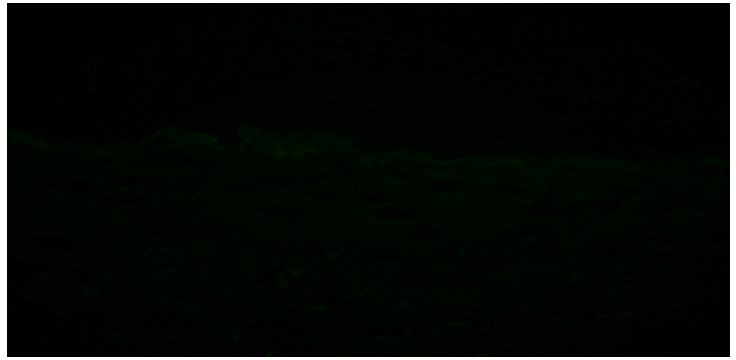
Baseline



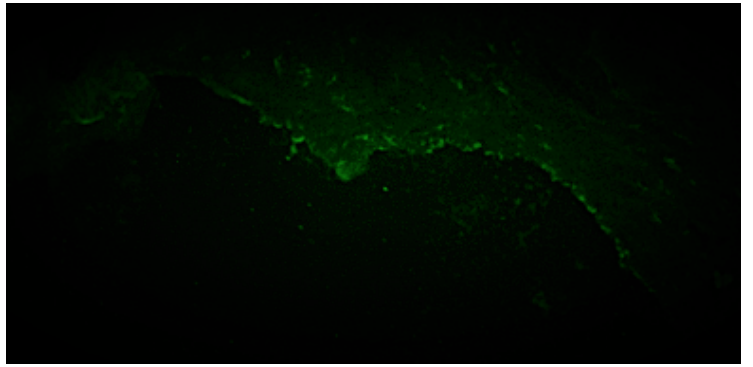
<-- NC1 -->



Baseline

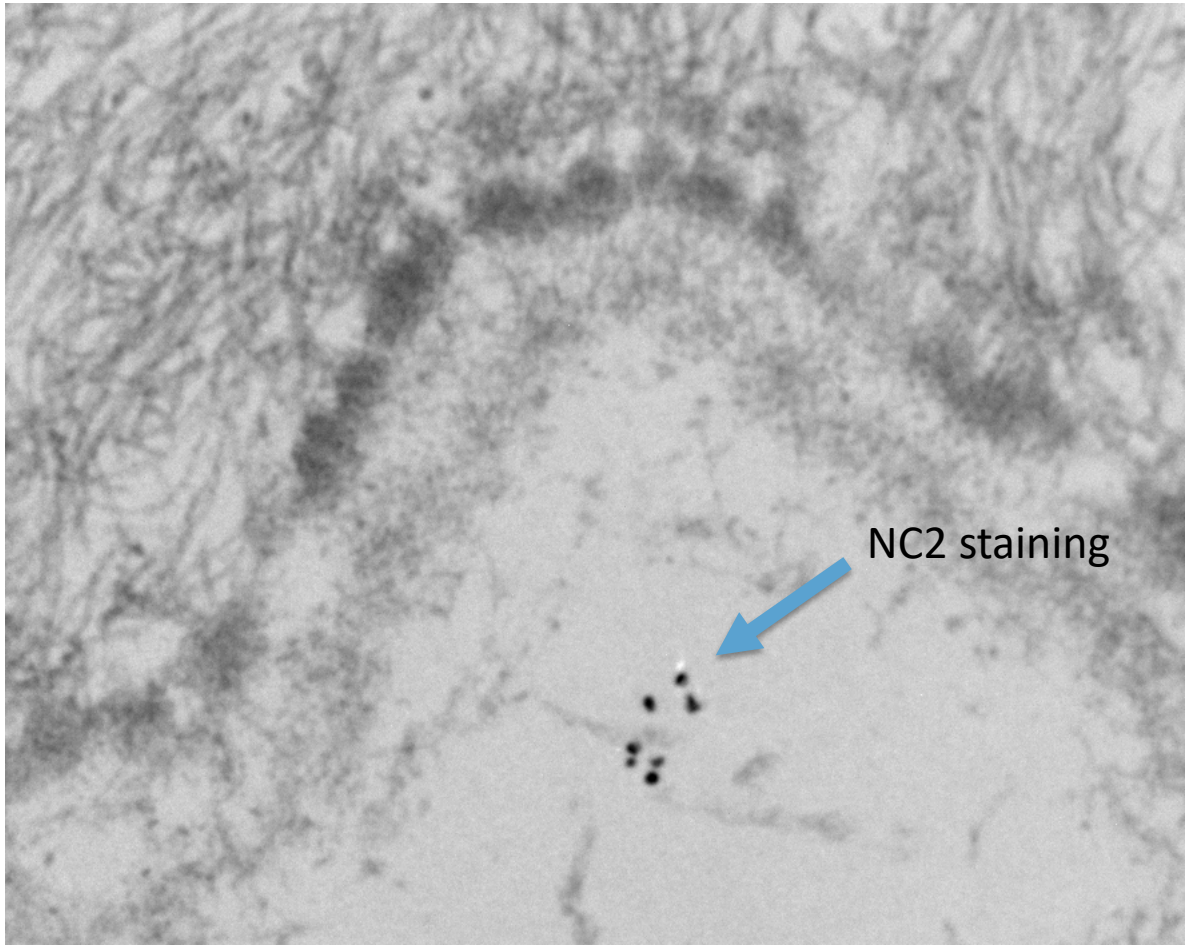


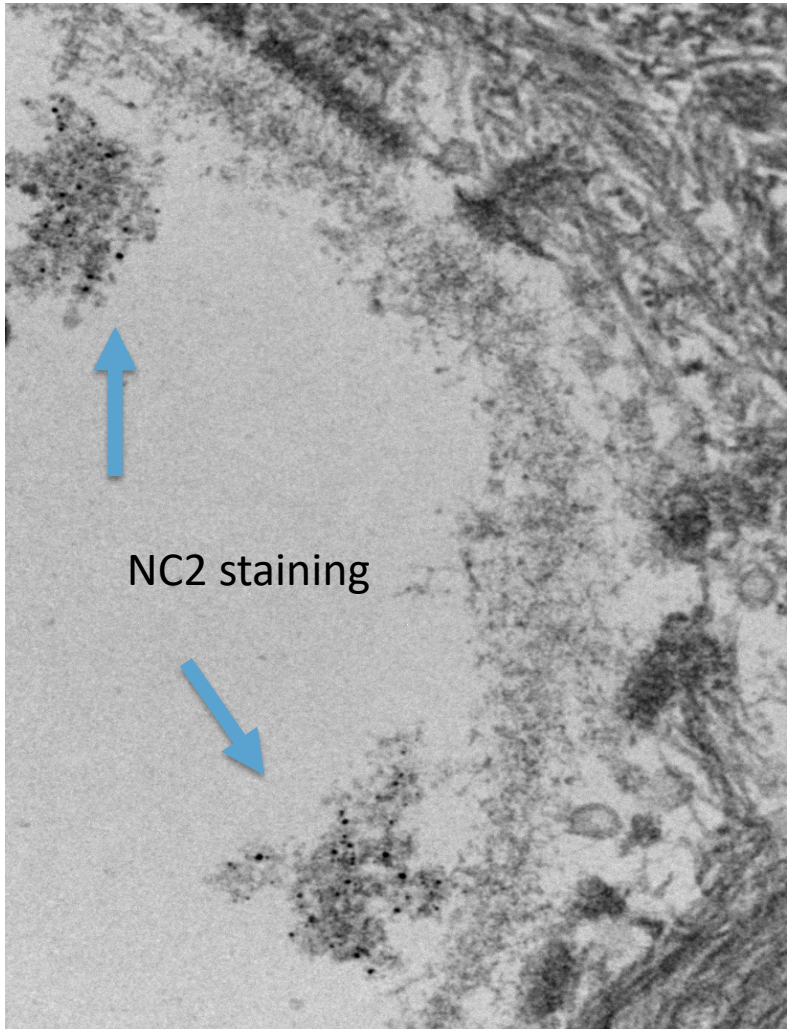
<-- NC2 -->



Anchoring fibrils

Immuno Electron Microscopy showing nascent anchoring fibril formation





KB103 Phase 2 Efficacy Summary

- In the Phase 2 study, 5 out of 6 wounds treated with KB103 closed completely (100% wound closure)
- The average time to 100% wound closure on 5 out 6 wounds was 23.4 days. On recurring wounds, the average time to 100% wound closure was 19 days.
- Duration following complete (100%) wound closure on recurring wounds as measured on Day 90 was therefore 71 days.
- Preliminary results indicate that duration of wound closure at 120 day timepoint was 101 days. We shall provide a further update on final duration of wound closure prior to commencing pivotal trials.
- Molecular correction was established in all 3 patients in Phase 2 trial and correlates to wound healing

KB103 Combined Summary Efficacy Update

- In the combined Phase 1 and Phase 2 study, 7 out of 8 wounds treated with KB103 closed completely (100%)

- The average time to 100% wound closure on all KB103 treated wounds in combined Phase 1 and Phase 2 study (7 out of 8) was 20.14 days (median 20 days).

- In Phase 1 study, the duration of wound closure on two patients following 100% wound closure as of the last follow up was 184 days (6.6 months) and 174 days (6.2 months).

- In Phase 2 study, preliminary results indicate that duration of wound closure at 120 day timepoint was 101 days. We shall provide a further update on duration of wound closure prior to commencing pivotal trials, once results are finalized.

Next Steps

Next Steps

- Recently enrolled two new patients:
  - Incrementally increase dosing frequency to treat chronic wounds
  - Gather additional information in preparation for designing a robust pivotal trial
- Anticipate commencing the pivotal trial before year end 2019 following discussions with the FDA
- Chemistry, Manufacturing and Control
  - Engineering run complete
  - Bioreactor manufacturing process finalized for PPQ run/Phase 3 clinical
  - Phase 3 clinical material manufacturing run to start in Q3, 2019