INTRODUCTION & BACKGROUND

Recessive dystrophic epidermolysis bullosa (RDEB) is an inherited genetic skin blistering disease caused by mutations in the COL7A1 gene encoding type VII collagen (C7) that results in dermal-epidermal separation. Current therapy for RDEB is limited to palliative wound care as there are no curative treatments and no approved drugs for RDEB. We report the results of the ongoing Phase 1/2 clinical trial of genetically-corrected, collagen VII expressing autologous human dermal fibroblasts (FCX-007) for the treatment of RDEB wounds (NCT02810951). The primary objective of this study is to evaluate the safety of intradermal injection of FCX-007. Secondary objectives are to evaluate clinical efficacy via percent wound healing compared to baseline and evaluate pharmacology via immunofluorescence (IF) and immunoelectron microscopy (IEM).

DEMOGRAPHICS

RESULTS

Safety

Interim data from the six subjects show that FCX-007 was well tolerated over 52 weeks post-administration with no antibody response to C7 detected after initial or repeat administration. No replication-competent lentivirus (RCL) and no C7 antibody responses have been noted in serum samples from subjects, including one subject with a negative NC-1 genotype.

Three subjects treated with FCX-007 had serious adverse events (SAE). Two subjects had SAES of squamous cell carcinoma (SCC) progression (not at the site by immunofluorescence) with one subject's SAE resulting in fatality. The SAES of SCC progression were deemed unrelated to the investigational product. One subject had an SAE of flu that resulted in hospitalization approximately one-month post-FCX-007 treatment that was deemed unrelated to the investigational product.

The injection procedure was well tolerated by all subjects. Erythema resulting in fatality. The SAEs of SCC progression were deemed unrelated to the investigational product.

Efficacy

Table 2. Treated Wound Healing Data

<table>
<thead>
<tr>
<th>Subject</th>
<th>Healing 6 Weeks</th>
<th>Healing 12 Weeks</th>
<th>Healing 25 Weeks</th>
<th>Healing 34 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 0101</td>
<td>80% (8/10)</td>
<td>90% (9/10)</td>
<td>75% (7/10)</td>
<td>67% (6/9)</td>
</tr>
<tr>
<td>Subject 0102</td>
<td>80% (8/10)</td>
<td>90% (9/10)</td>
<td>75% (7/10)</td>
<td>67% (6/9)</td>
</tr>
<tr>
<td>Subject 0103</td>
<td>80% (8/10)</td>
<td>90% (9/10)</td>
<td>75% (7/10)</td>
<td>67% (6/9)</td>
</tr>
</tbody>
</table>

Table 3. Untreated Wound Healing Data

<table>
<thead>
<tr>
<th>Subject</th>
<th>Healing 6 Weeks</th>
<th>Healing 12 Weeks</th>
<th>Healing 25 Weeks</th>
<th>Healing 34 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 0101</td>
<td>20% (2/10)</td>
<td>44% (4/9)</td>
<td>0% (0/4)</td>
<td>0% (0/4)</td>
</tr>
</tbody>
</table>

Digital images captured and wound tracings performed. Skin tattoos and transparent overlays were used as landmarks. Matched untreated wound was also monitored in conjunction with each treated wound on the same patient. Wounds were assessed for percent wound healing compared to baseline.

Figure 1. Gene-corrected Autologous Fibroblasts (FCX-007)

(A) COL7A1 gene is delivered to a patient via a retroviral vector.

(B) Fibroblasts are expanded in the laboratory.

(C) Fibroblasts isolated from RDEB patient skin biopsies.

(D) Fibroblasts expanded and transduced with SIV lentiviral vector encoding COL7A1.

METHODS

Six subjects, five adults and one child, with severe generalized RDEB (ages 9 to 38 at age of enrollment) were dosed with FCX-007. The subjects carried various COL7A1 mutations resulting in undetectable C7 expression with one microcopy and a lack of anchoring fibrils (AF) by electron microscopy (EM) (Table 1). The therapy was administered in the margins of and across targeted chronic wounds, ranging in size from 4.3 to 34.1 cm², as well as in separate intact skin sites. Persistent non-healing wounds were targeted to assess efficacy of wound healing (categorical scale: 0%, 1-9%, 10-24%, 25-49%, 50-74%, 75-89%, 90-99% and 100% healed) and pharmacology via IF and IEM. All six subjects received a single treatment session at baseline. Four subjects received a second treatment session at 52, 25, 12, and 4 weeks post-baseline administration; subjects 0102, 0103, 0105 and 0106, respectively.

CONCLUSIONS

In this interim data set, FCX-007 was well tolerated up to 52 weeks post-administration. Injections of both wounded and intact skin were well tolerated without safety issues, including a lack of immune or RCI related events. Positive wound healing trends and pharmacology signals were observed for up to 52 weeks of testing. These results informed the design of the phase 3 DEF-RDEB study (NCT04213261).