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Abstract #1540

# Robust Pre-Clinical Results and Large-Scale Manufacturing Process for EDIT-301: An Autologous Cell Therapy for the Potential Treatment of SCD

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## Disclosures

- Employees and shareholders of Editas Medicine:  
E.D., J.H., P.S., T.J., H.A., C.F.A., S.T., T.M., K.Z., K-H.C.
- Nothing to disclose:  
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# Introduction



## EDIT-301

is an autologous cell therapy comprising **CD34<sup>+</sup> cells** from **patients with SCD (sickle cell disease)** that are **edited with CRISPR-Cas12a** at the **HBG1 and HBG2 promoters** to induce the expression of anti-sickling fetal hemoglobin

## Objectives:

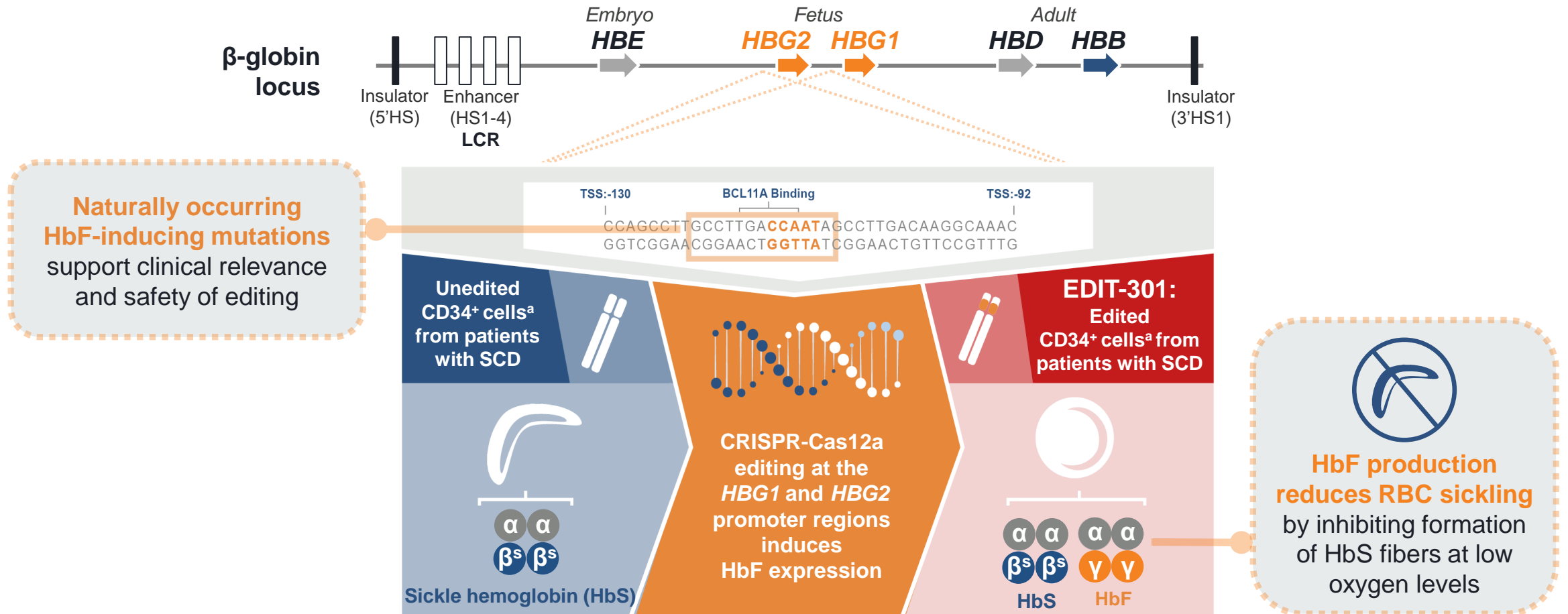


To demonstrate the **function and phenotype** of edited red blood cells (RBCs) derived from EDIT-301 *in vitro*



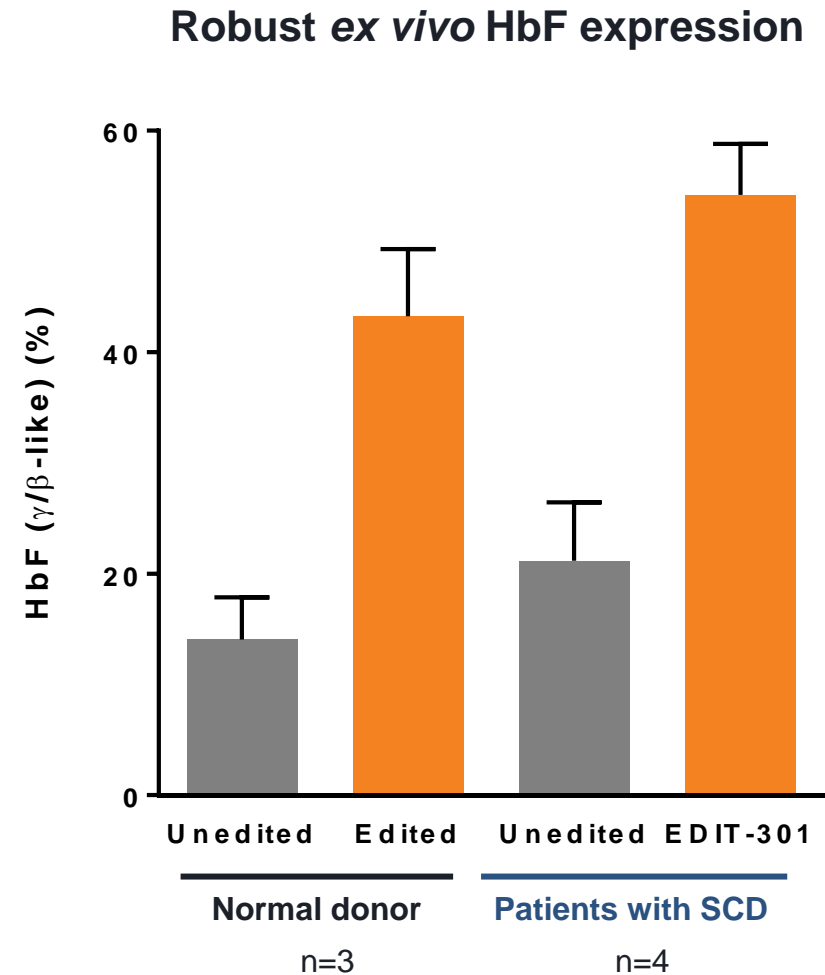
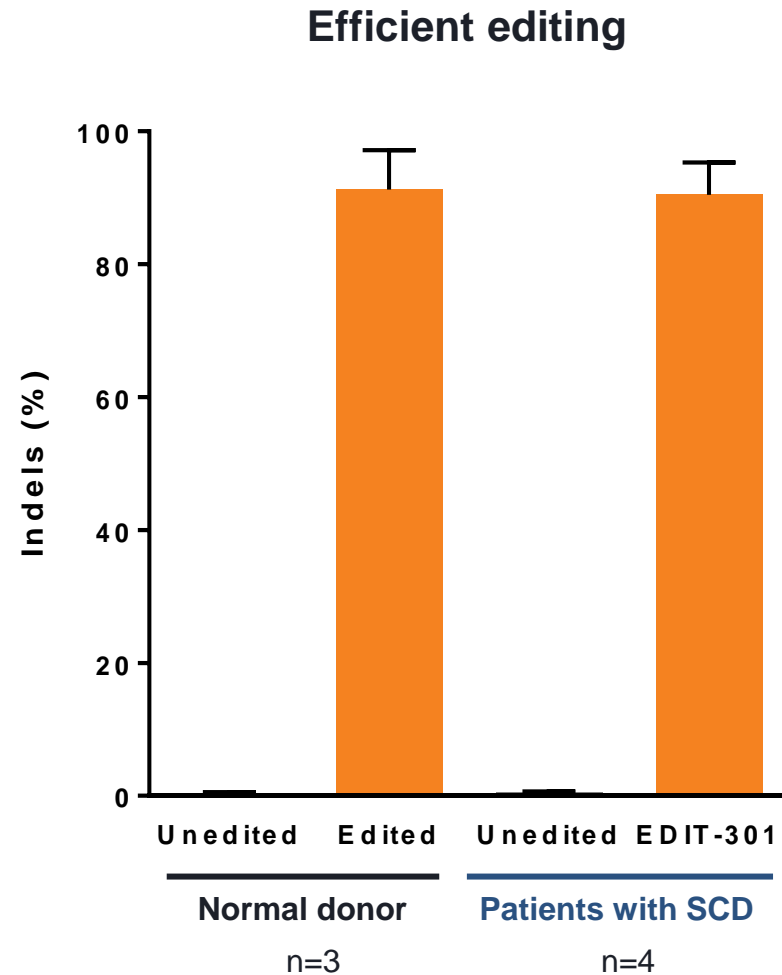
To evaluate the edited CD34<sup>+</sup> cell **large-scale manufacturing process**

# CRISPR-Cas12a editing at the *HBG1* and *HBG2* promoter regions induces anti-sickling fetal hemoglobin (HbF) to treat SCD



<sup>a</sup>CD34<sup>+</sup> hematopoietic stem and progenitor cell  
 HS: hypersensitive site; LCR: locus control region; TSS: transcriptional start site  
 Adapted from Higgs, Engel and Stamatoyannopoulos. *Lancet* 2012

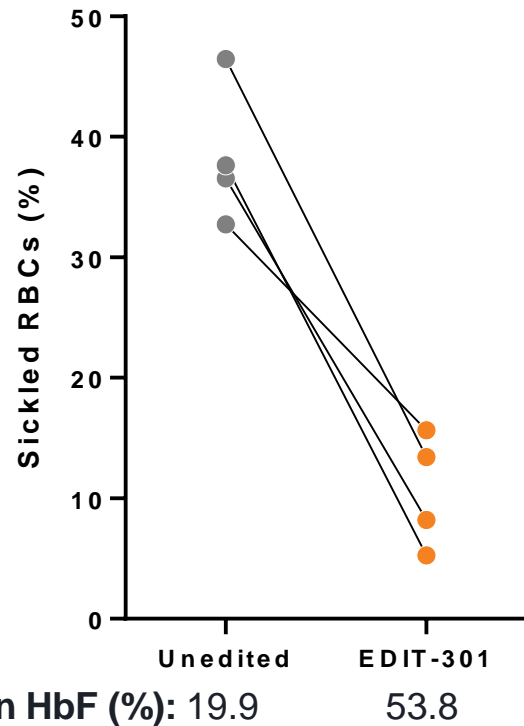
# Comparable editing and robust HbF induction in edited CD34<sup>+</sup> cells from normal donors and patients with SCD



Unedited cells did not undergo electroporation

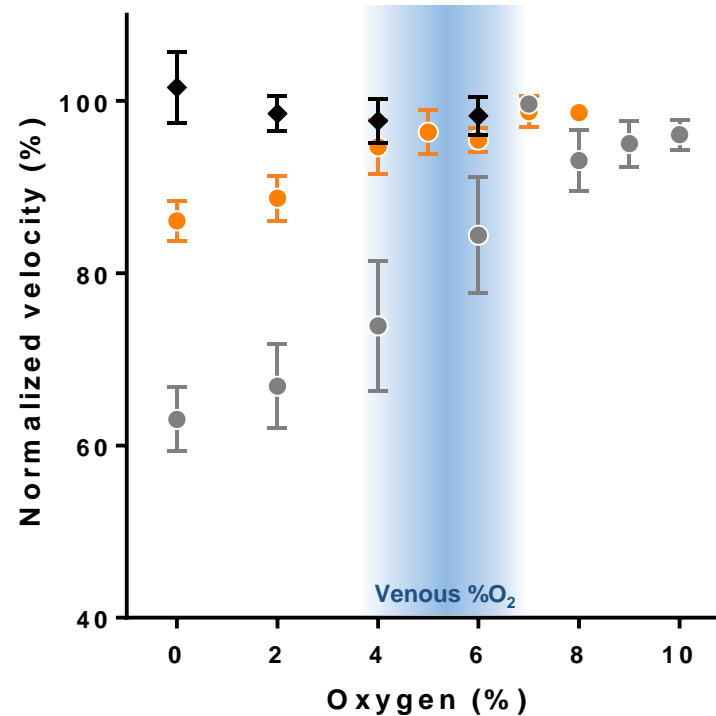
# EDIT-301-derived RBCs have reduced sickling and improved rheological properties versus unedited SCD-derived RBCs

Reduced sickling



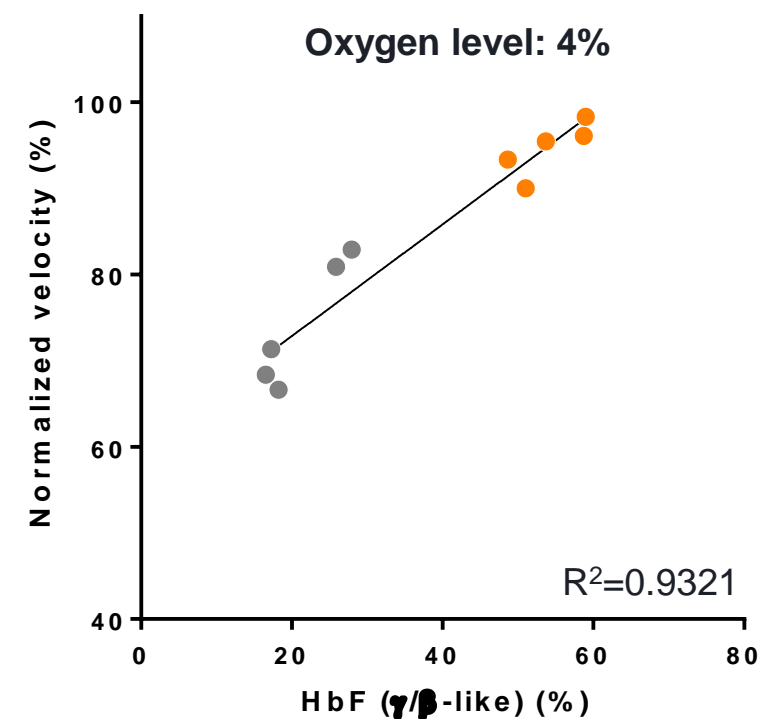
When exposed to sodium metabisulfite

Improved rheological behavior



When placed in microfluidic channels, mimicking blood flow in microvasculature, at a range of oxygen levels

HbF levels correlated with velocity

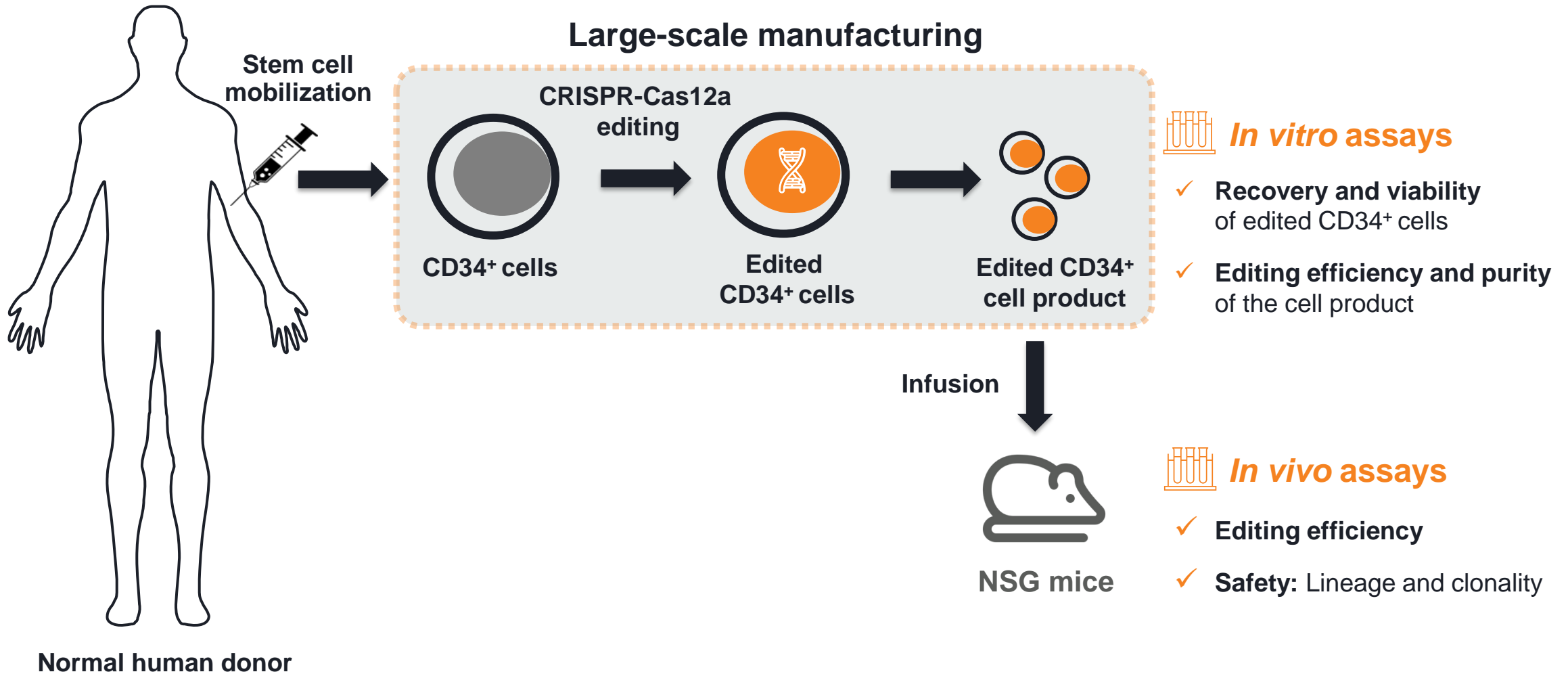


◆ Normal donor-derived RBCs

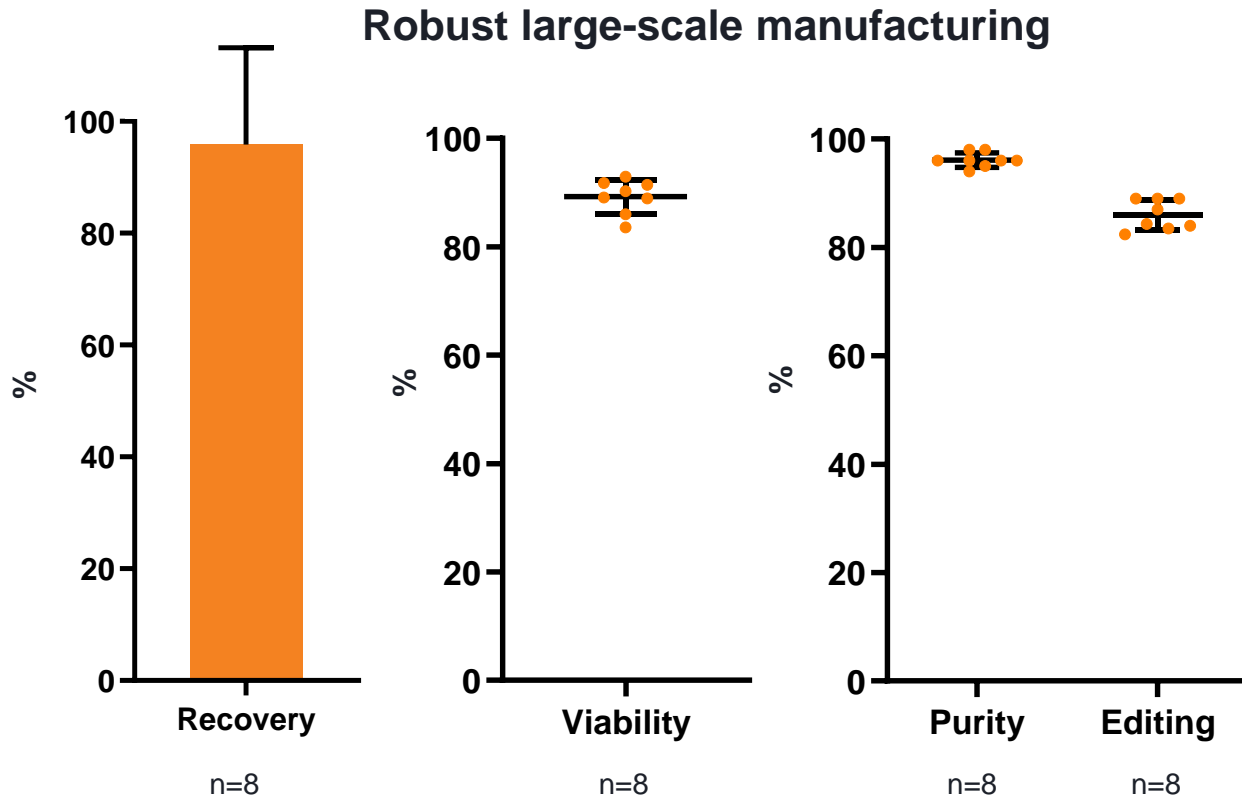
● Unedited SCD-derived RBCs

● EDIT-301 (edited SCD)-derived RBCs

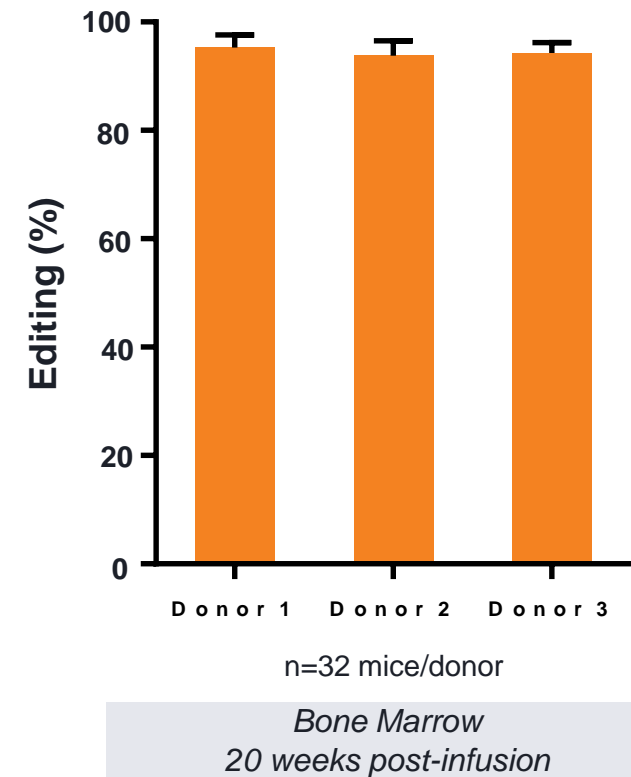
# Successful development of edited CD34+ cell large-scale manufacturing process



# Consistent and robust large-scale manufacturing of edited CD34<sup>+</sup> cells from normal donors



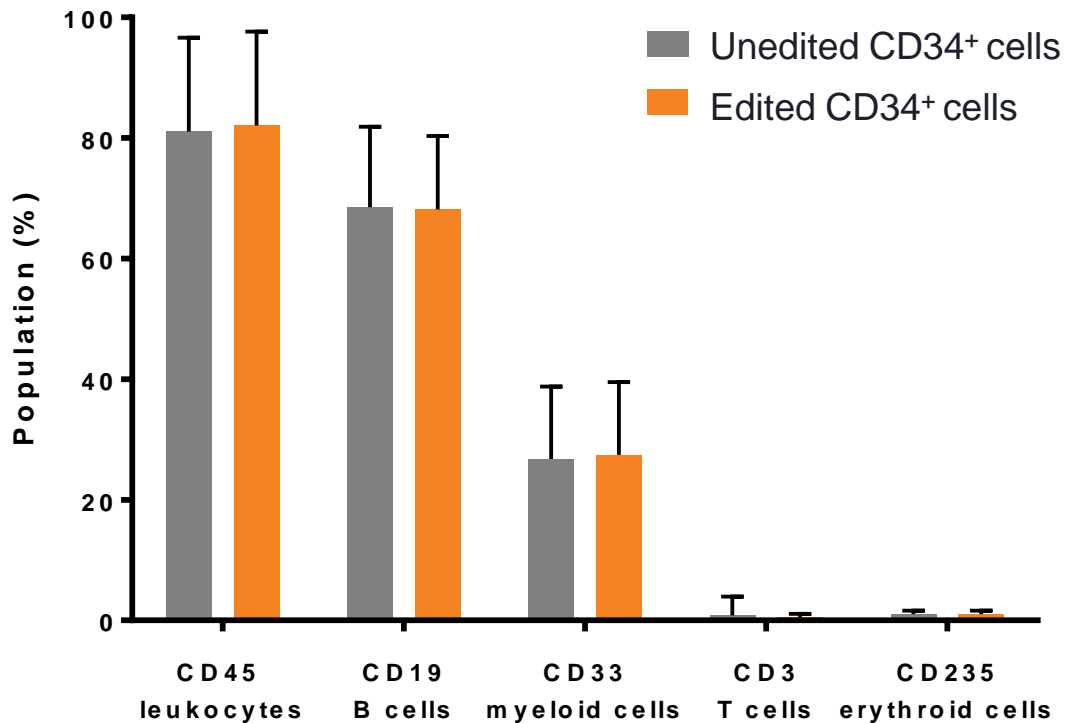
### Efficient editing maintained *in vivo*





# Infusion of edited CD34<sup>+</sup> cells manufactured on a large scale to NSG mice leads to polyclonal engraftment with no lineage skewing

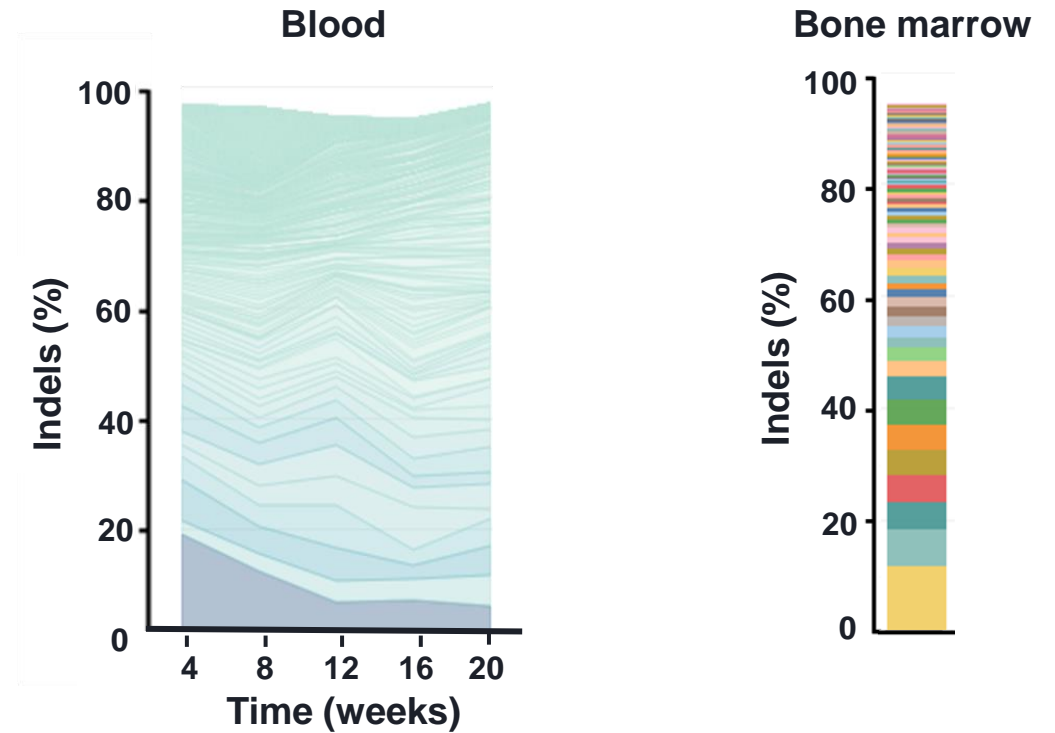
### No lineage skewing after engraftment



Female NSG mice bone marrow 20 weeks post-infusion

n=46–48 mice/treatment

### Stable polyclonal engraftment



Blood draws over 20 weeks

20 weeks post-infusion

Representative data from one NSG mouse.  
Each color or color shade represents an individual indel signature.

# Conclusions

High levels of editing were achieved in CD34<sup>+</sup> cells, leading to **potentially therapeutically relevant levels of HbF** expression

**Significant reduction in sickling** and **improved rheological properties** of EDIT-301 (edited SCD)-derived RBCs

**Consistent large-scale process suitable for use in clinical manufacturing** showing multilineage, polyclonal engraftment, and persistence of high levels of editing *in vivo*

**Plan to file Investigational New Drug application** for EDIT-301 by end of 2020

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