# PROVIDING HOPE TO UNDERSERVED PATIENTS

Global Blood Therapeutics, Inc.

January 2018

GBT

Hope + Science + Community

# SAFE HARBOR STATEMENT

Statements we make in this presentation may include statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. We intend these forward-looking statements, including statements regarding the therapeutic potential and safety profile of voxelotor (previously called GBT440), our ability to implement and complete our clinical development plans for voxelotor, our ability to generate and report data from our ongoing and potential future studies of voxelotor (including our ongoing Phase 3 Hope Study and our ongoing HOPE-KIDS 1 Study), regulatory review and actions relating to voxelotor, our ability to adequately obtain and protect our intellectual property rights, and the timing of these events, to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Securities Exchange Act and are making this statement for purposes of complying with those safe harbor provisions. These forward-looking statements reflect our current views about our plans, intentions, expectations, strategies and prospects, which are based on the information currently available to us and on assumptions we have made. We can give no assurance that the plans, intentions, expectations or strategies will be attained or achieved, and furthermore, actual results may differ materially from those described in the forward-looking statements and will be affected by a variety of risks and factors that are beyond our control including, without limitation, the risks that our clinical and preclinical development activities may be delayed or terminated for a variety of reasons, that results of clinical trials may be subject to differing interpretations, that regulatory authorities may disagree with our clinical development plans or require additional studies or data to support further clinical investigation of our product candidates, that drug-related adverse events may be observed in clinical development, and that data and results may not meet regulatory requirements or otherwise be sufficient for further development, regulatory review or approval, along with those risks set forth in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the U.S. Securities and Exchange Commission. Except as required by law, we assume no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

# POSITIONED TO DELIVER INNOVATIVE TREATMENTS TO UNDERSERVED PATIENT COMMUNITIES

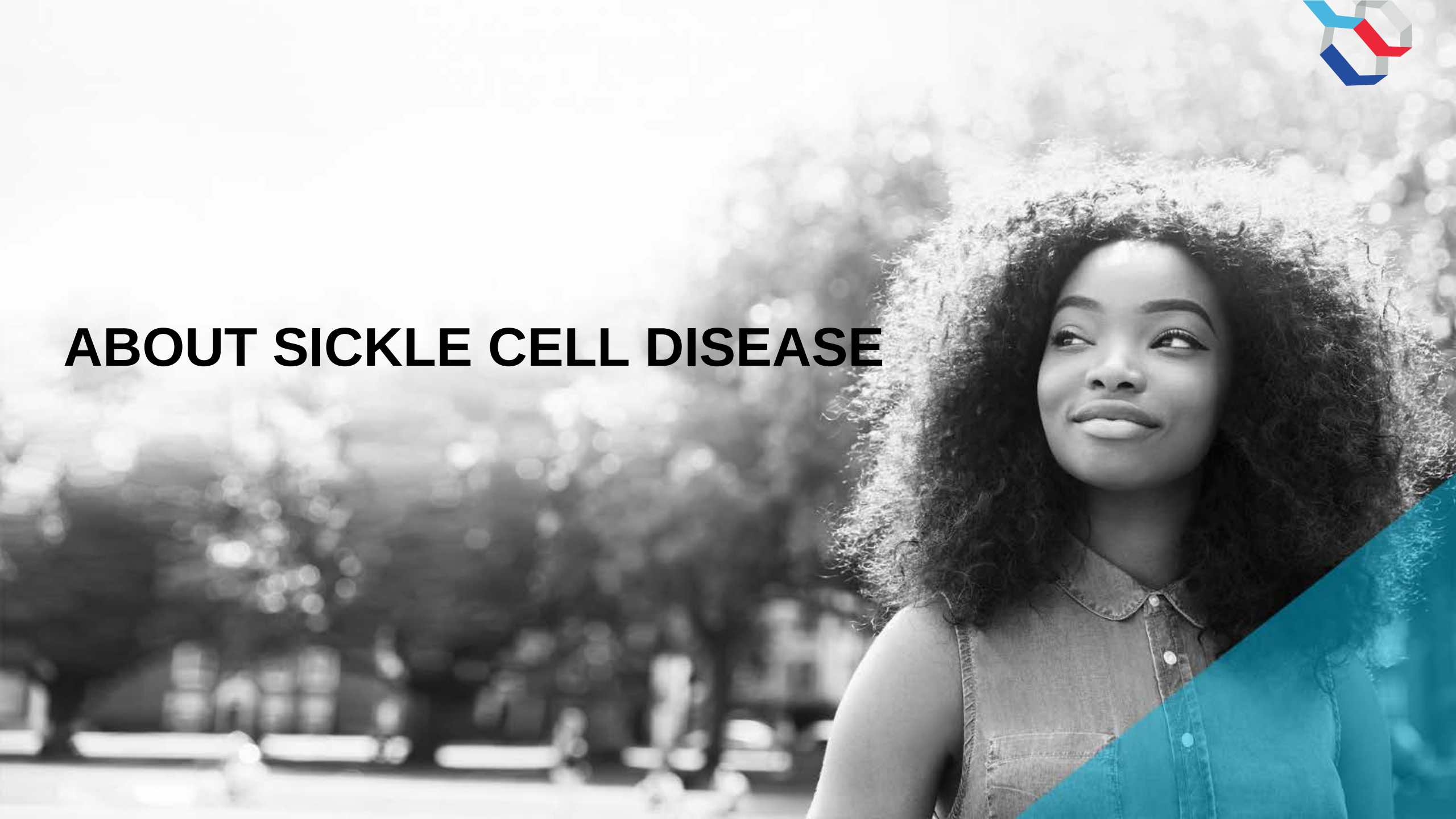
## Voxelotor: Breakthrough Therapy

+ First and only SCD treatment to receive FDA Breakthrough Therapy Designation
  - **FDA**: Fast Track, Orphan Drug & Rare Pediatric Disease
  - **EMA**: Orphan Drug & PRIME
  - Ongoing HOPE Study; Part A data in 1H'18
  - Ongoing HOPE-KIDS 1 (007) study in children age 6-17

## Foundation for Growth

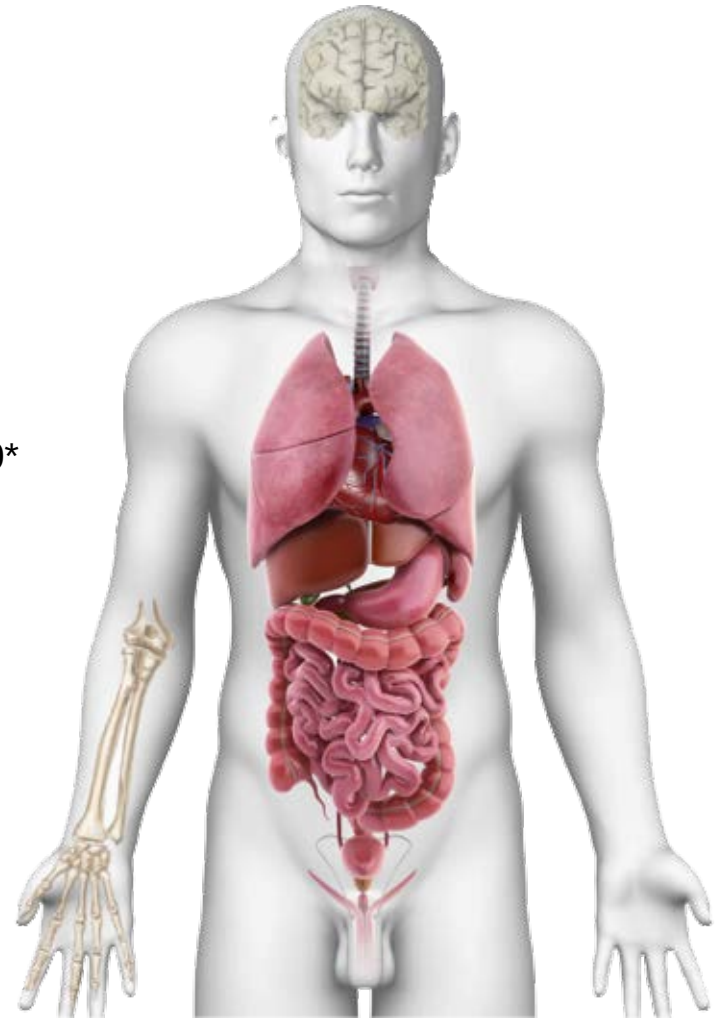
+ Wholly controlled product portfolio with composition of matter beyond 2032
+ $259.4M cash, cash equivalents and marketable securities as of 9/30/2017 *(excludes $110.8M from recent public offering)*
+ Pipeline expansion
  - Internal R&D efforts
  - Active business development team

# ABOUT SICKLE CELL DISEASE



# SCD: DISABLING INHERITED BLOOD DISORDER

- **Devastating morbidity and mortality**
  - Vaso-occlusion, hemolytic anemia, inflammation/vascular injury
  - Results in multi-organ damage
  - 2 to 3 decade reduction in life expectancy
  - Current treatments are severely limited
- **Orphan indication**
  - ~100,000 patients in U.S.; ~60,000 in EU
  - U.S. average annual costs per patient for care exceeds ~$200,000*
  - Efficient commercial footprint
- **Voxelotor is uniquely suited to address unmet need**
  - Oral therapy
  - Disease modifying
  - Excellent safety and tolerability profile



**No Organ Spared**
**Common Morbidities**

**Brain**
Cerebral infarcts, strokes
Thrombosis or hemorrhage causing paralysis, sensory deficits or death

**Lung**
Acute chest syndrome
Pulmonary hypertension
Pneumonia

**Kidney**
Hematuria
Renal insufficiency
Renal failure

**Bones and joints**
Bone marrow hyperplasia
Osteomyelitis
Avascular necrosis/osteonecrosis

**Eye**
Hemorrhage
Retinal detachment
Blindness
Retinopathy

**Heart**
Cardiomegaly
Heart failure

**Spleen**
Splenic atrophy(autosplenectomy)

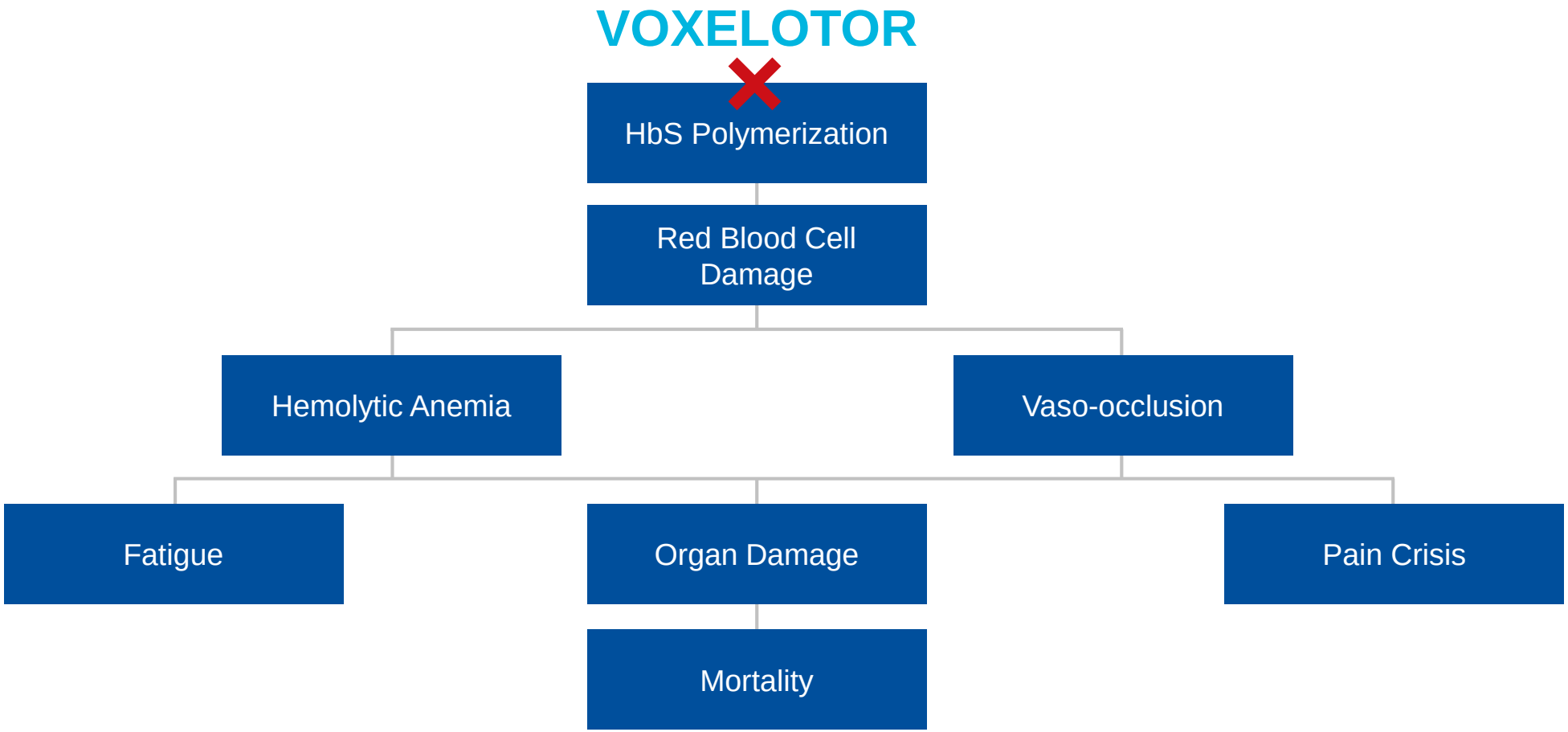
**Liver-gallbladder**
Hepatomegaly
Gallstones

**Skin**
Stasis ulcers of hands, ankles and feet

**Men/Women**
Priapism
Adverse pregnancy outcomes

*Source: *The cost of health care for patients with sickle cell disease,* Ballas, Samir K., 2009, American Journal of Hematology http://www3.interscience.wiley.com/cgi-bin/jhome/35105

# VOXELOTOR INHIBITS ABNORMAL HBS POLYMERIZATION, THE FUNDAMENTAL CAUSE OF SCD PATHOPHYSIOLOGY




*Eaton W, Bunn F. Targeting HbS Polymerization, Blood 2017.*

# 001: PHASE 1/2 CLINICAL STUDY IN ADULTS

# 001: STUDY DESIGN -- CHRONIC DOSING FOR 90 DAYS AND BEYOND

**001: Phase 1/2, Randomized, Double-blind, Placebo-controlled Study in Adult HbSS, HbS/β0thalassemia, HbS/β+thalassemia, or HbSC Patients**

**Part A – Single Dose**

+ Healthy volunteers: 5 cohorts (100, 400, 1000, 2000, 2800 mg)
+ SCD patients: 1 cohort (1000 mg)

**Part B – Multiple Doses (15 and 28 days)**

+ Healthy volunteers: 3 cohorts (300, 600, 900 mg per day x 15 days)
+ SCD patients: 3 cohorts (500 mg, 700 mg, 1000 mg per day x 28 days)

**Part C – Multiple Doses (90 days)**

+ SCD patients: 2 cohorts (700 mg, 900 mg per day x 90 days)

***Cohorts = 8 people (6 active, 2 placebo)****

**Objectives**

+ Pharmacokinetics
+ Pharmacodynamics
+ SCD patients: hematologic parameters
+ Safety

**024 (open-label extension study)**

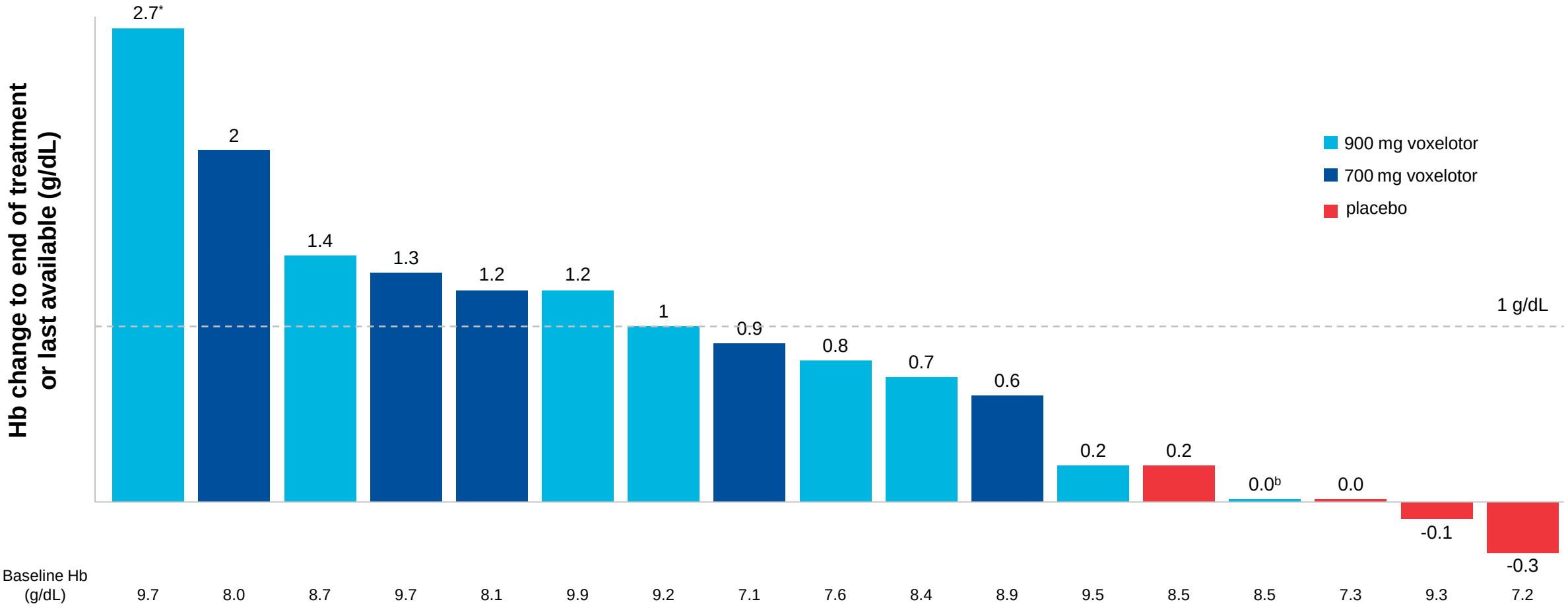
Extended dosing of voxelotor (Cohort 17, 900 mg) for a total of 6 months

*Except SCD patients in Part B: 500 mg cohort (10:4); 700 mg cohort (12:4)

# 001: EFFICACY SUMMARY

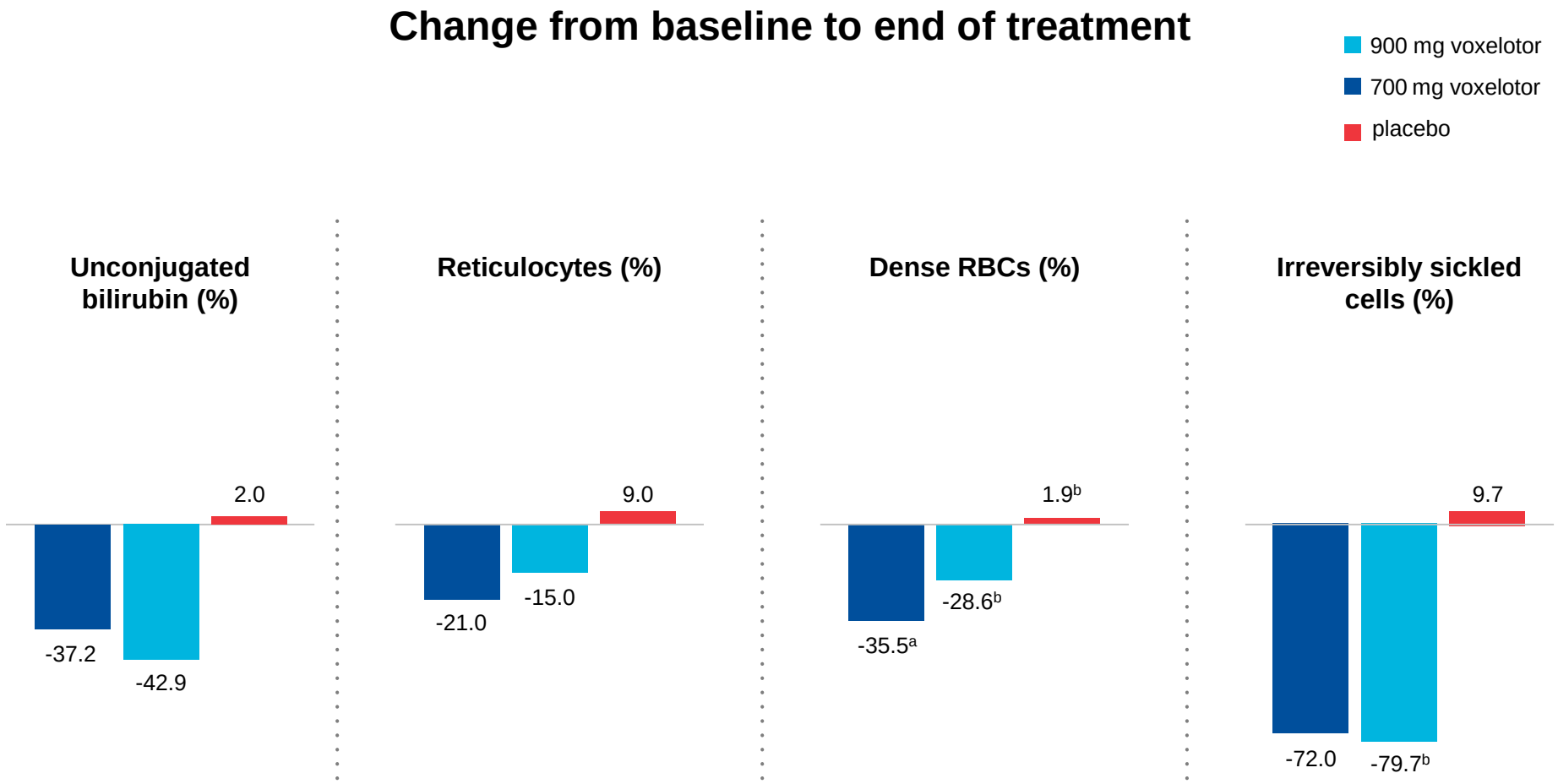
- **100% of SCD patients in all cohorts** (N= 41) dosed with voxelotor for 28 days up to 6 months **have shown hematologic response** (Hb, reticulocytes and/or bilirubin)
- Longer-term dosing up to 6 months shows reduction in hemolysis and peripheral blood sickle cells, consistent with earlier findings
  - **46% of voxelotor-treated patients show** a clinically significant **increase in hemoglobin (>1g/dL)** vs 0% placebo ($p$ =0.006)
  - **77% median decline in irreversibly sickled cells in voxelotor-treated patients** vs. 10% increase in placebo ($p$<0.001)
- The treatment response data are consistent with *in vivo* inhibition of HbS polymerization

# 001: 46% OF PATIENTS ACHIEVE HEMOGLOBIN RESPONSE >1 G/DL




*Day 15 data presented due to a protocol-specified dose reduction on Day 17 because of a large increase in Hb
**Patient documented non-adherence with study drug regimen

# 001: ALL PATIENTS DOSED WITH VOXELOTOR SHOWED A REDUCTION IN HEMOLYSIS, RETICULOCYTES AND/OR SICKLE CELLS




[a]Data available for n=4
[b]Data available for n=5

# 001: SAFETY AND TOLERABILITY PROFILE

- **Voxelotor was well tolerated**
- **No serious or severe adverse events**
- **No evidence of tissue hypoxia**
  - No increase in erythropoietin
  - No decrease in $O_2$ consumption with exercise

# PHASE 2a HOPE-KIDS 1 Study (007)

## Interim Results Evaluating Adolescents with SCD Treated with Multiple Doses of Voxelotor

# 007: STUDY DESIGN

## HOPE-KIDS 1 (007): Phase 2a Open-label, Single- and Multiple-dose Clinical Trial in Pediatric Population

### Part A – Single Dose

+ Cohort 1: SCD patients age 12-17: 600 mg
+ Cohort 2: SCD patients age 6 -11: 600 mg

### Part B – Multiple Doses

+ Cohort 1: SCD patients age 12-17: 900 mg per day x 24 weeks
    - ***ASH oral presentation provided interim results (16 weeks)***
+ Cohort 2: SCD patients age 12-17: 1500 mg per day x 24 weeks

### Objectives

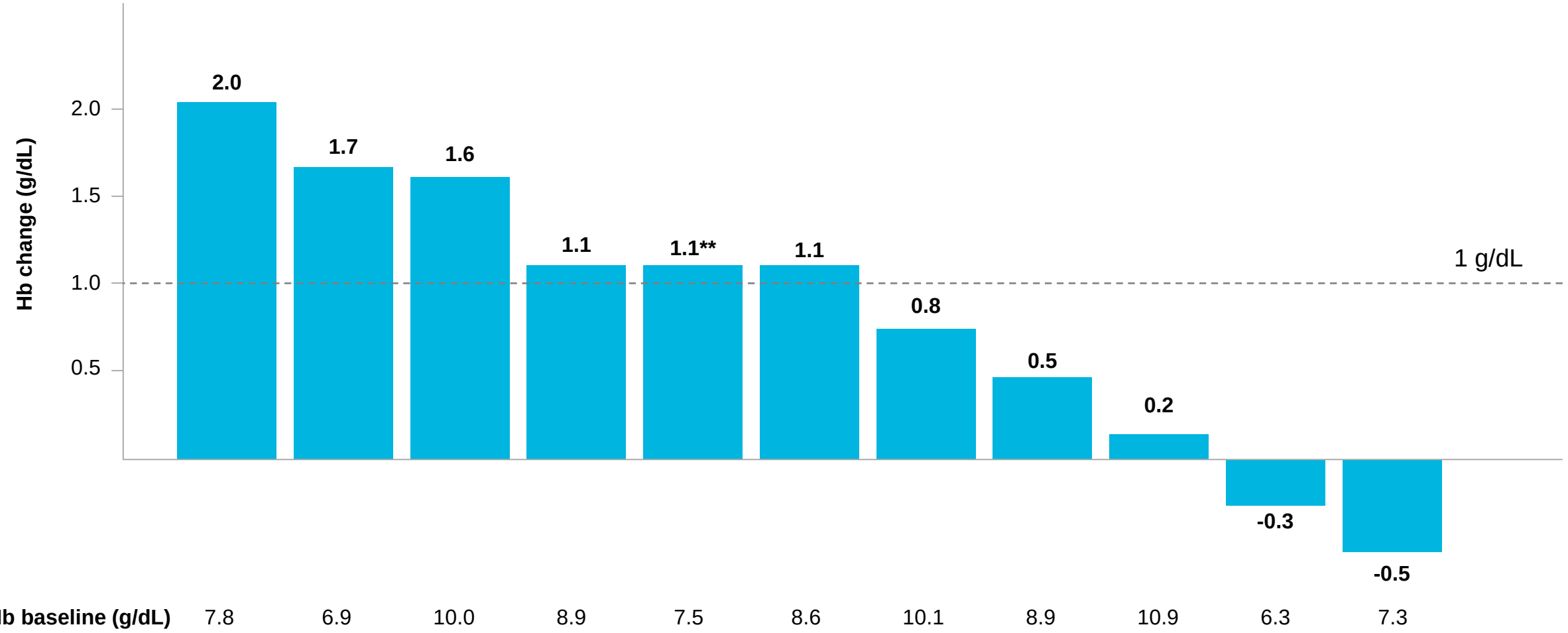
+ Assess efficacy as measured by improvement in anemia
+ Effect on clinical measures of hemolysis
+ Effects on total symptom score (TSS) from PRO
+ Pharmacokinetics
+ Safety/tolerability

# 007: BASELINE CHARACTERISTICS (Data as of November 6, 2017)

| Baseline Characteristics | 900 mg N=24 All treated patients to date (Safety population) | 900 mg N=12 16 weeks treated (Efficacy population) |
|---|---|---|
| Male n (%) | 14 (58) | 6 (50) |
| Age (years, median, range) | 14 (12-17) | 13 (12-17) |
| HbSS genotype*, n (%) | 23 (96) | 11 (92) |
| Number of VOCs in prior year, n (%) | | |
| 0 | 11 (46) | 7 (59) |
| 1-4 | 11 (46) | 4 (33) |
| >4 | 2 (8) | 1 (8) |
| Baseline Hb (g/dL, median, range) | 8.9 (6.3-11.0) | 8.7 (6.3-10.9) |
| Current hydroxyurea use, n (%) | 21 (88) | 11 (92) |
| Baseline HbF (%, median, range) | 11.2 (3.7-29.0) | 10.7 (5.5-29.0) |

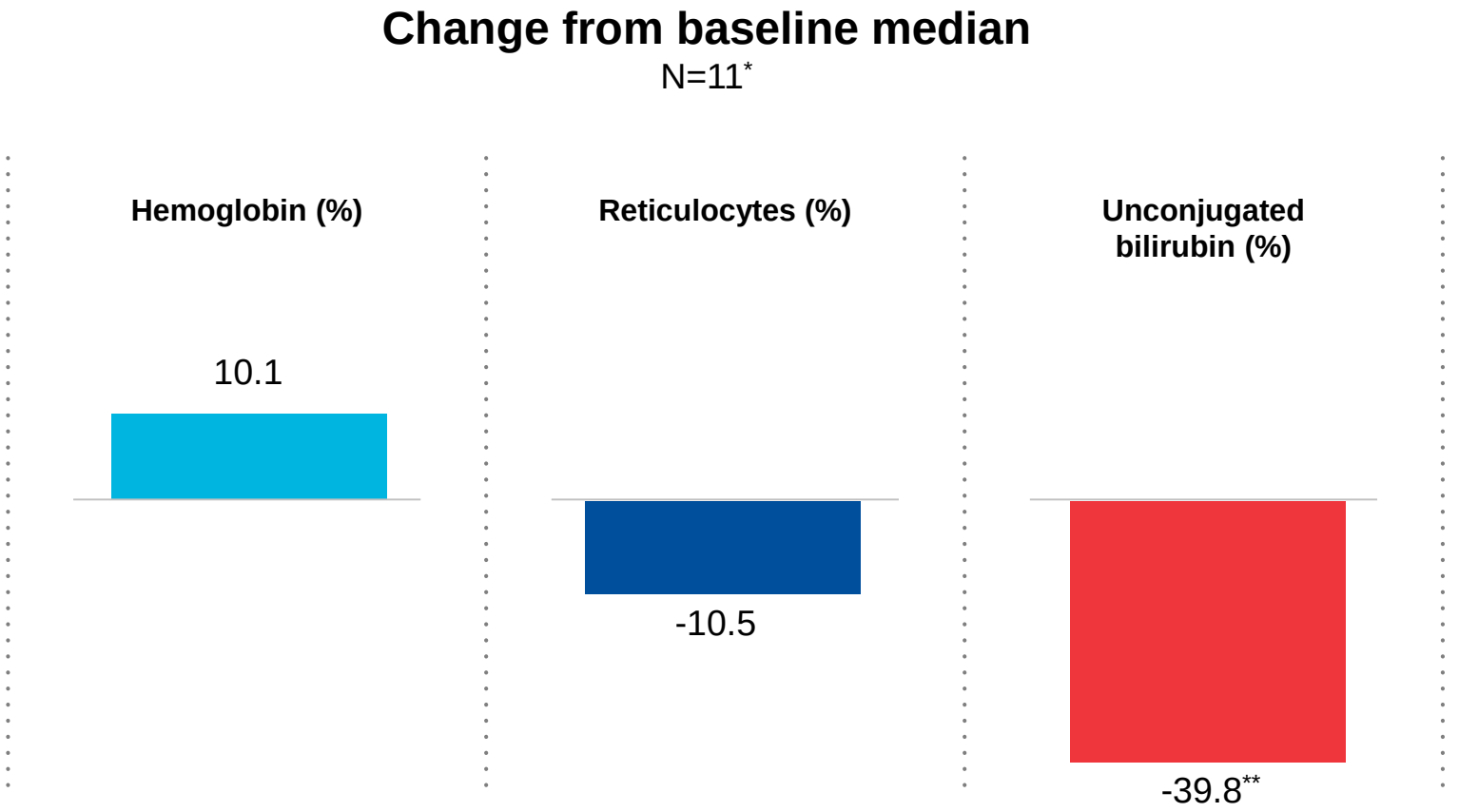
**One patient with HbS $\beta^0$ thal*

# 007: 55% OF PATIENTS ACHIEVED HEMOGLOBIN RESPONSE >1 G/DL AT 16 WEEKS*




*Data not available on one patient at 16 weeks
**Not on concurrent HU

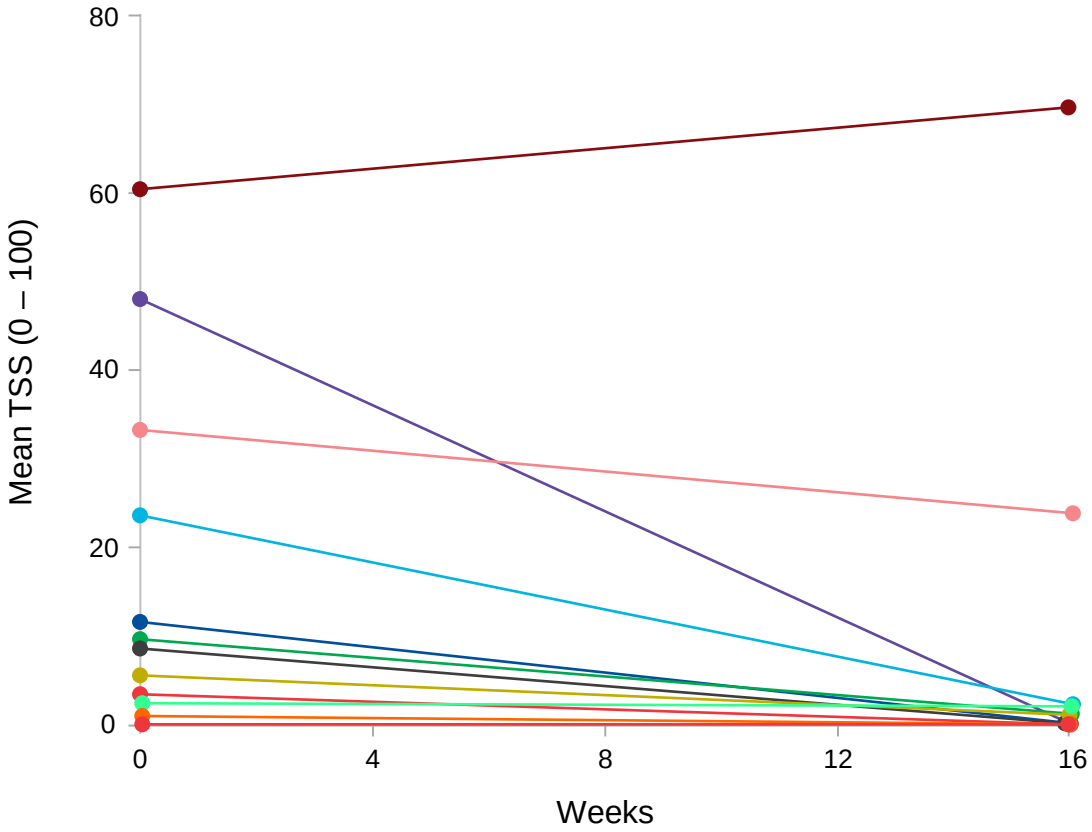
# 007: HEMOLYSIS MEASURES AT 16 WEEKS




*Data not available on one patient at 16 weeks
**n=10

# 007: REDUCED TOTAL SEVERITY SCORE AT WEEK 16

- 10 of 12 patients showed reduction in TSS from baseline
- 94% median reduction in TSS from baseline
- 5 of 12 patients had a mean TSS of 0




**Each dot represents mean daily TSS averaged over preceding study period**
(2 week screening and 12-16 week treatment)

# 007: SAFETY AND TOLERABILITY

- Voxelotor 900 mg was well tolerated
- Drug-related AEs related to voxelotor were Grade 1 or 2 (except one Grade 3 rash*)
- No drug-related SAEs
- No study drug discontinuations due to AEs

*Did not recur with continued dosing

# HOPE STUDY

**H**emoglobin **O**xygen Affinity Modulation to Inhibit HBS **P**olym**E**rization

A randomized, double-blind, placebo-controlled, multi-national, Phase 3 study

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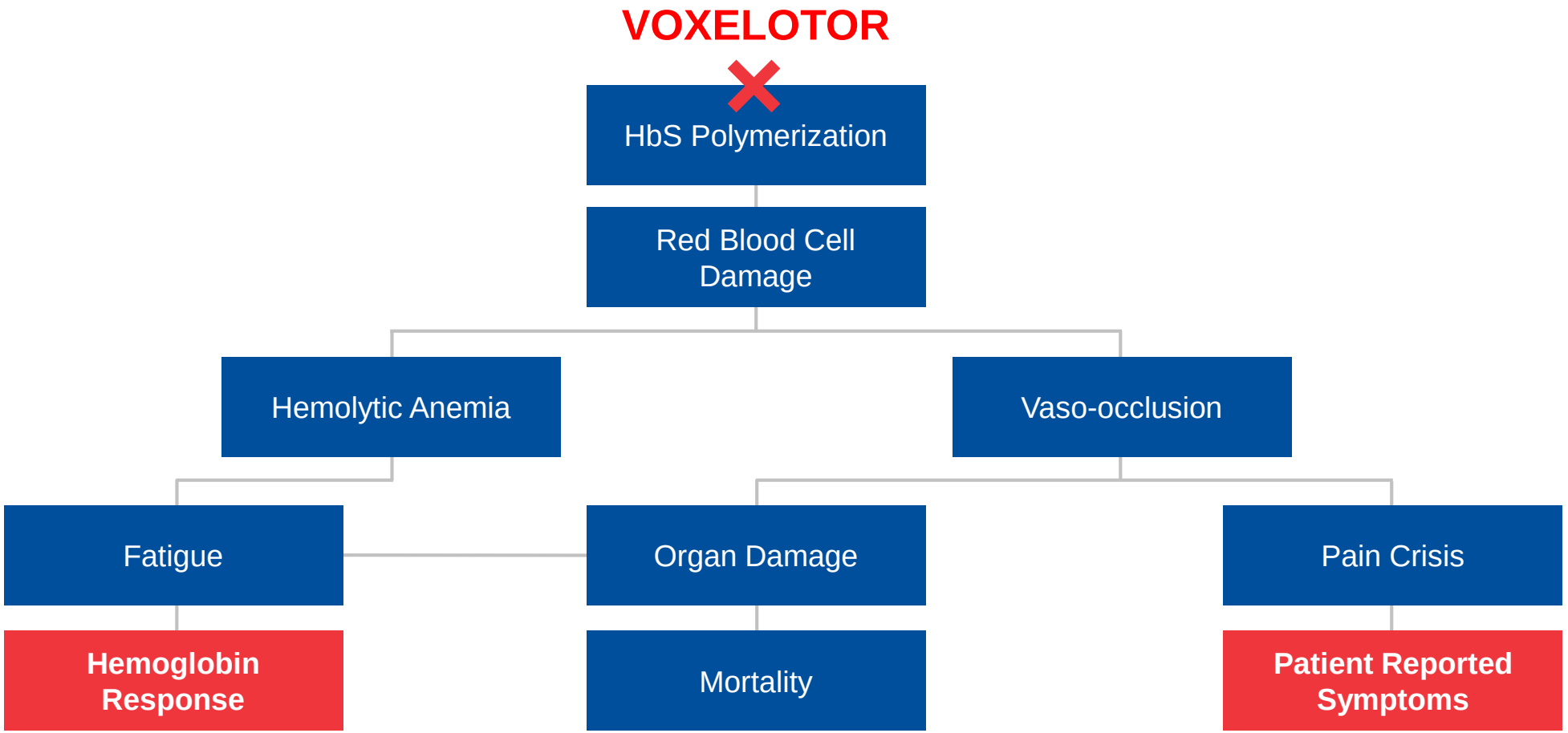



*Eaton W, Bunn F. Targeting HbS Polymerization, Blood 2017.*

# PHASE 3 HOPE STUDY DESIGN HAS STRONG GROUNDING IN VOXELOTOR MECHANISM OF ACTION

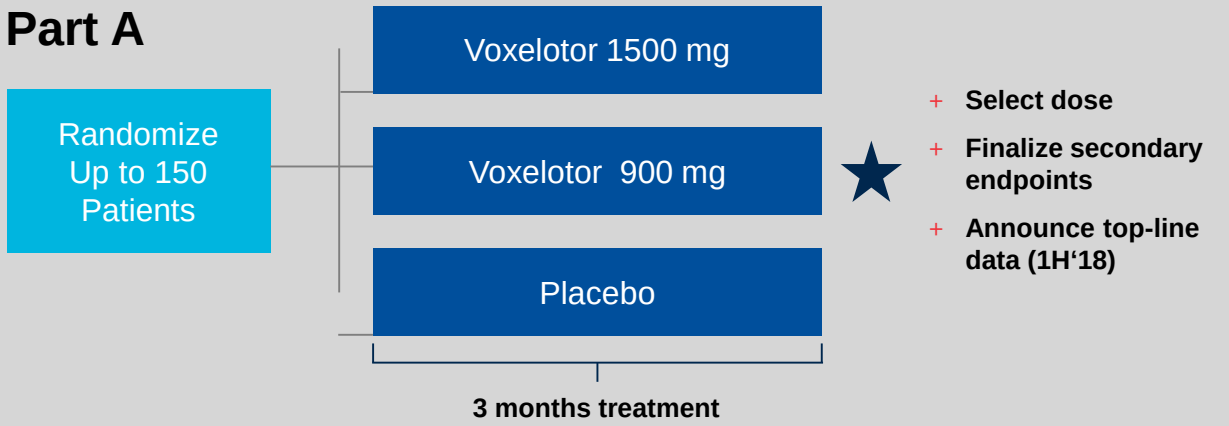
HOPE
Sickle Cell Disease Clinical Study

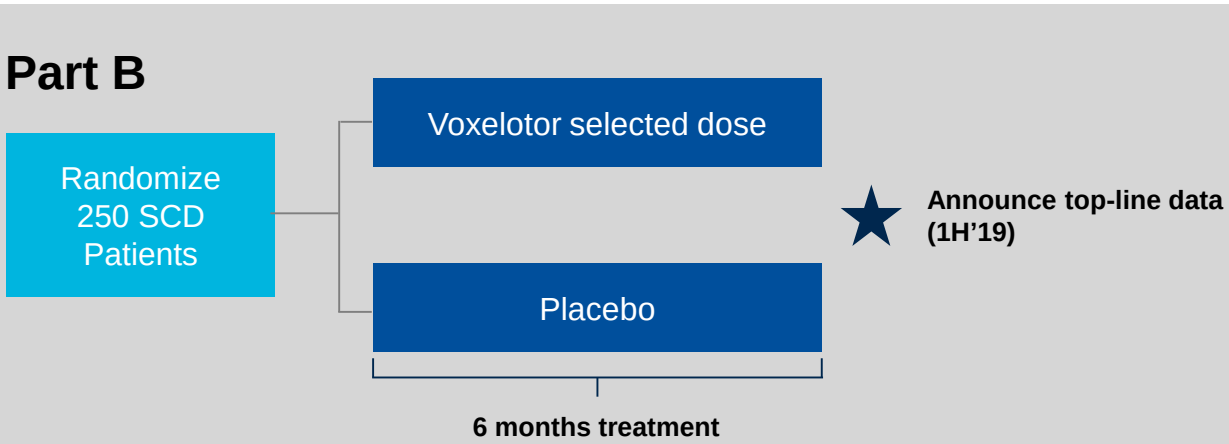
**SCD Patient Population**:

- 1-10 VOCs in prior year
- Baseline Hb ≤10.5 g/dL
- ≥12 years old
- Concomitant hydroxyurea allowed

**Endpoints:**

- Primary: Proportion of patients who achieve a >1 g/dL Hb improvement at week 24
- Key Secondaries: PRO exacerbation days and/or Total Symptom Score, VOC requiring a HCP interaction, hospitalizations



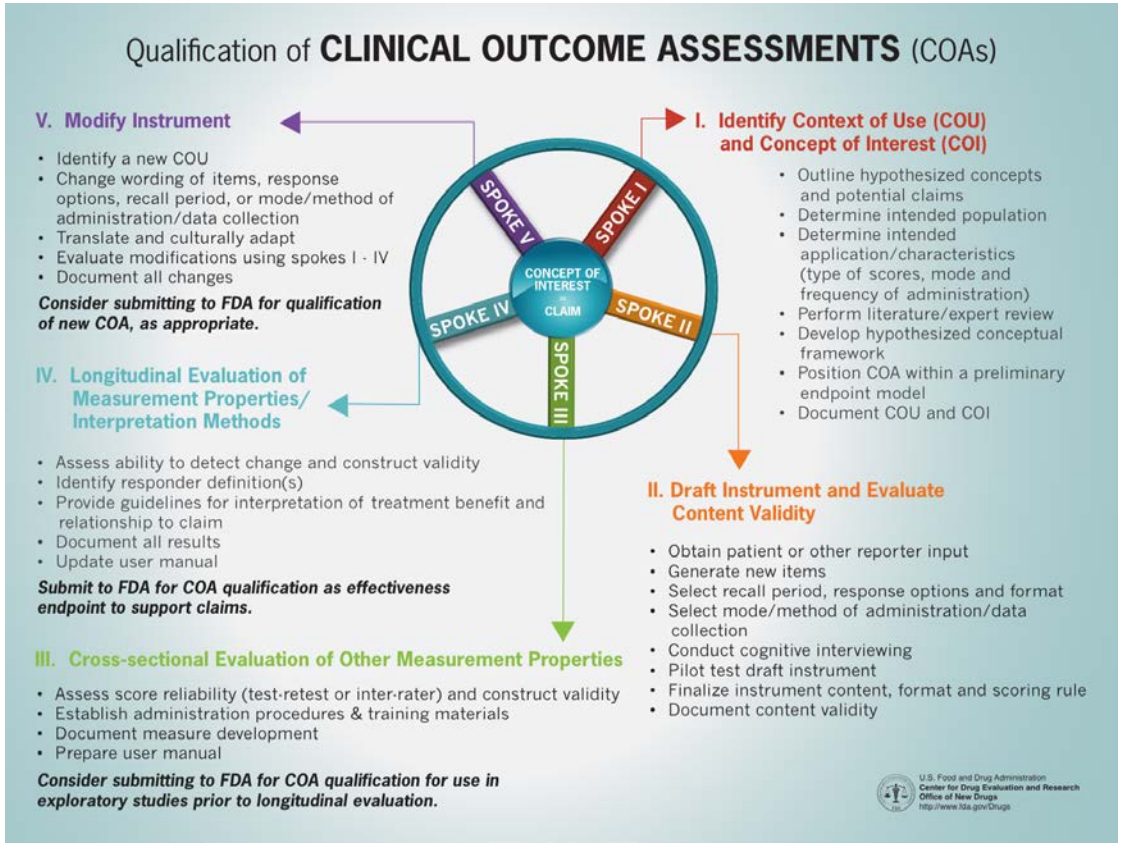



# POTENTIAL KEY SECONDARY ENDPOINT

Patient Reported Outcomes (PRO) Tool

# QUALIFICATION OF PRO AS A CLINICAL OUTCOMES ASSESSMENT

## FDA Guidelines



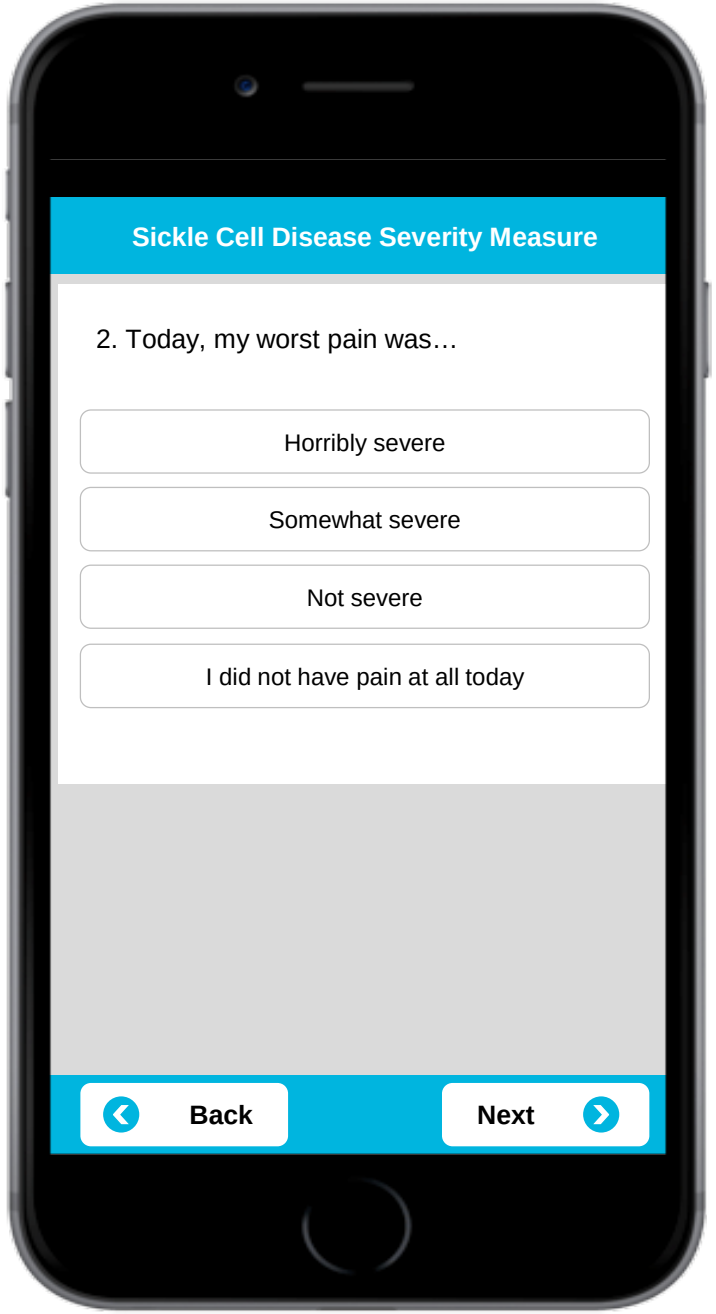

## GBT's PRO Development Status

+ Context of use and concept of interest:
  SCD severity measure for use as a clinical outcomes assessment for labeling purposes
+ Draft instrument with content validity:
  9 item measure, daily recall, translation and cultural adaptation
+ Cross-sectional evaluation:
  established reliability and measurement properties

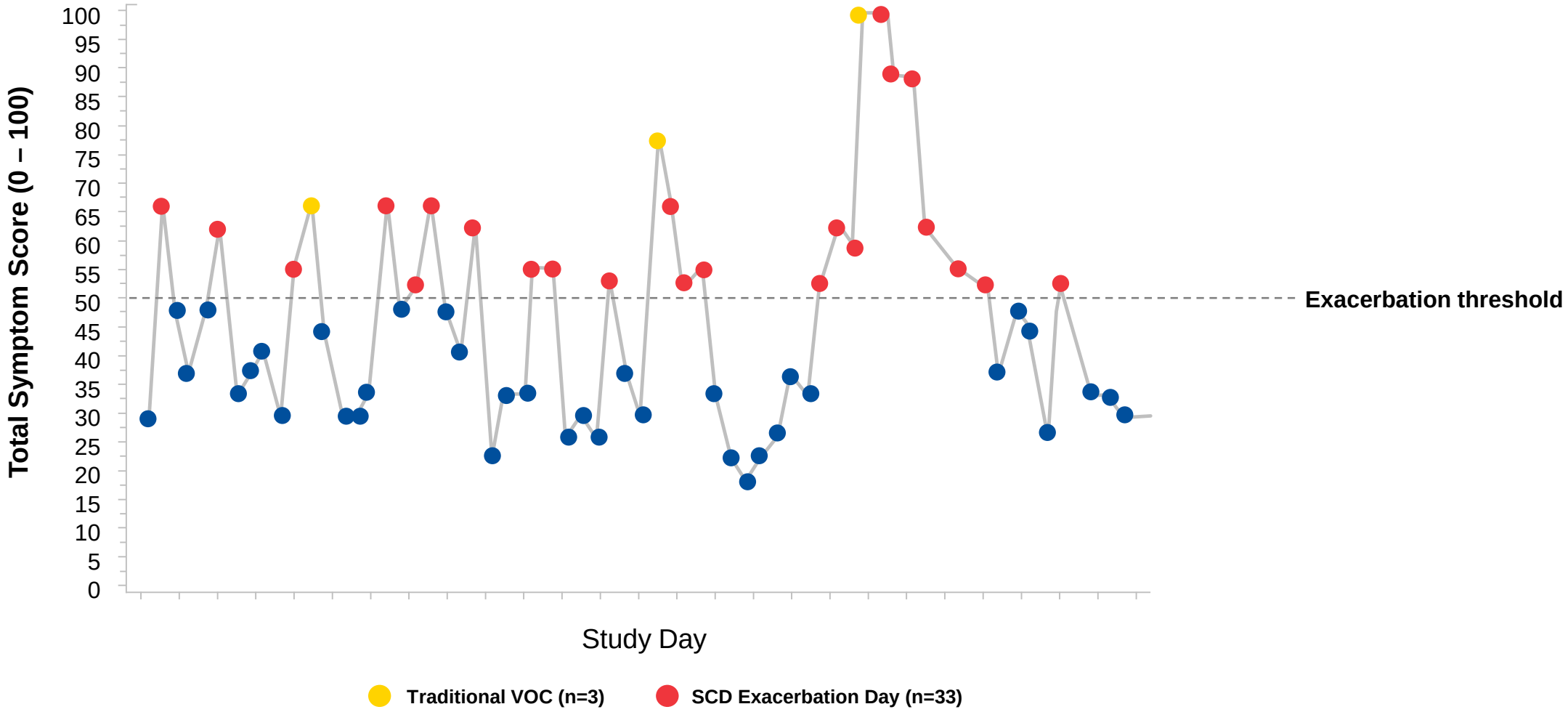
## Outstanding Items to be Agreed to with FDA After HOPE Study Part A Analysis

+ Responder definition
+ Guidelines for endpoint evaluation

# GBT’S NOVEL PRO

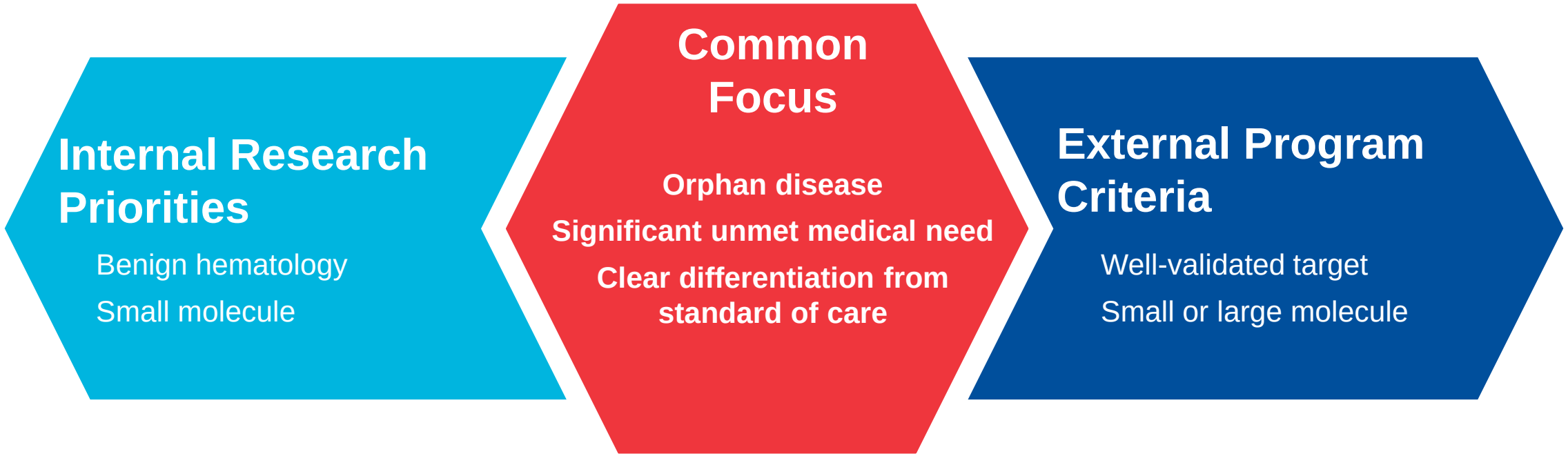


# PRO MAY PROVIDE MORE POWER THAN VOC BY CAPTURING PATIENT-REPORTED CRISIS EPISODES



# POSITIONED FOR GROWTH

# CRITERIA TO EXPAND OUR PIPELINE



# MAJOR VALUE DRIVERS IN 2018 AND BEYOND

**Voxelotor: Sickle Cell Disease**

- ✓ Breakthrough Therapy Designation received from FDA
- ✓ Enrolling adult and adolescent patients with SCD in HOPE Study
- **1H ’18** Part A top-line results from HOPE Study
- **1H ’18** HOPE-KIDS 1 Study complete results (900 mg)
- **2H ’18** HOPE-KIDS 1 Study top-line results (1500 mg)
- **1H ’19** Part B top-line results from HOPE Study

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# Q&A

Breakout Location: Yorkshire Room

NASDAQ: GBT

GBT

Hope + Science + Community