

# ASH 2016 Highlights Innovations In Sickle Cell Disease

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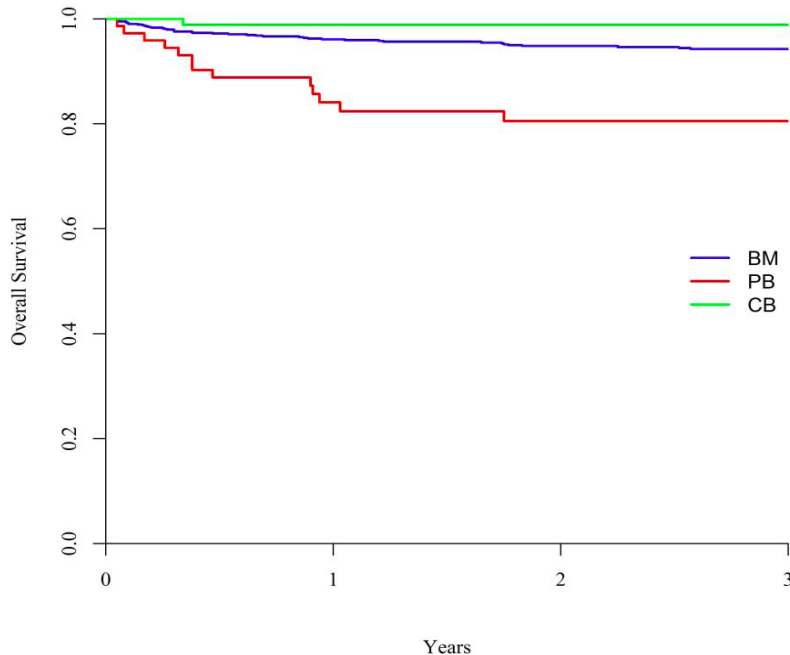
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# The path to achieving a cure for SCD?

## Stem Cell Transplantation

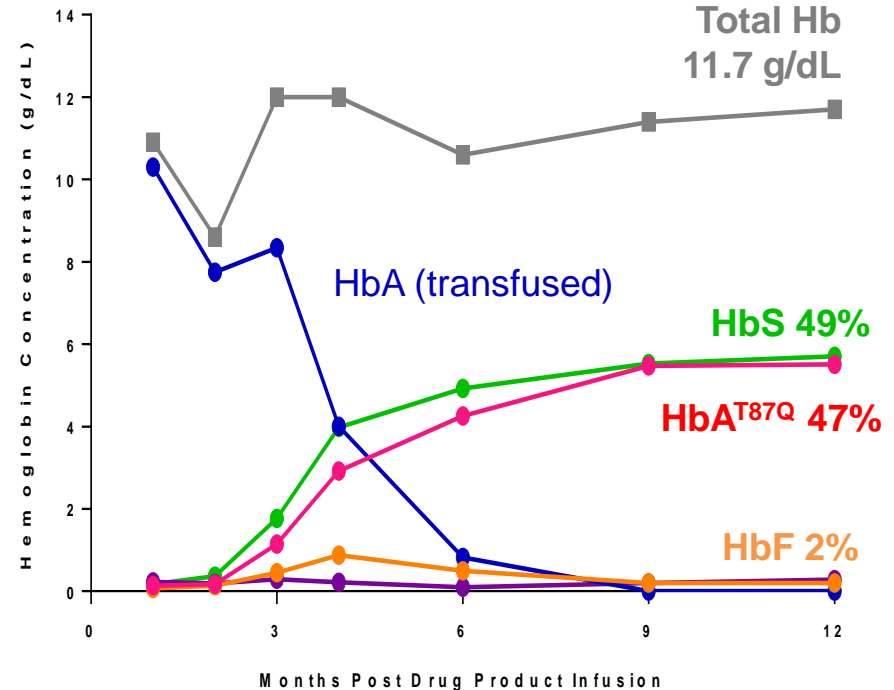
- Data from 1000 children with SCD from Europe, Brazil, United States, Africa and the Middle East who underwent stem cell transplants from matched, sibling donors



94% Overall Survival @3Y

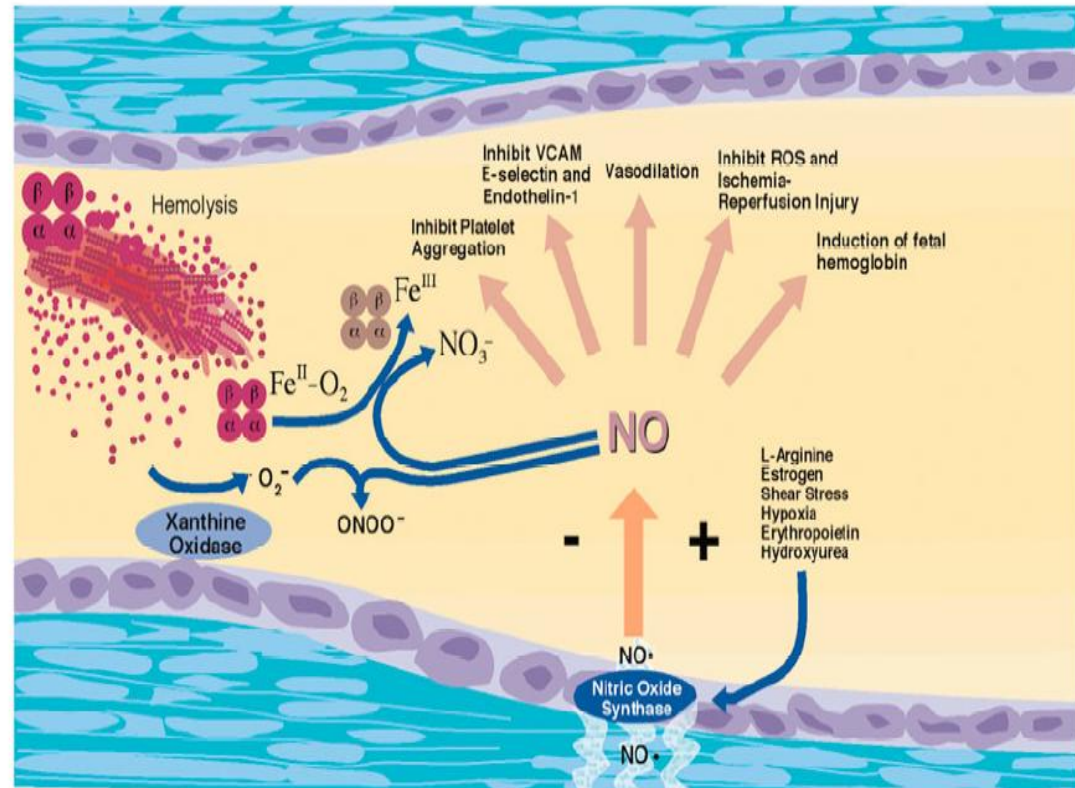
## Gene Therapy

- Patient serves as own donor
- Engineered viral vector used to insert normal copy of single gene that is defective in SCD

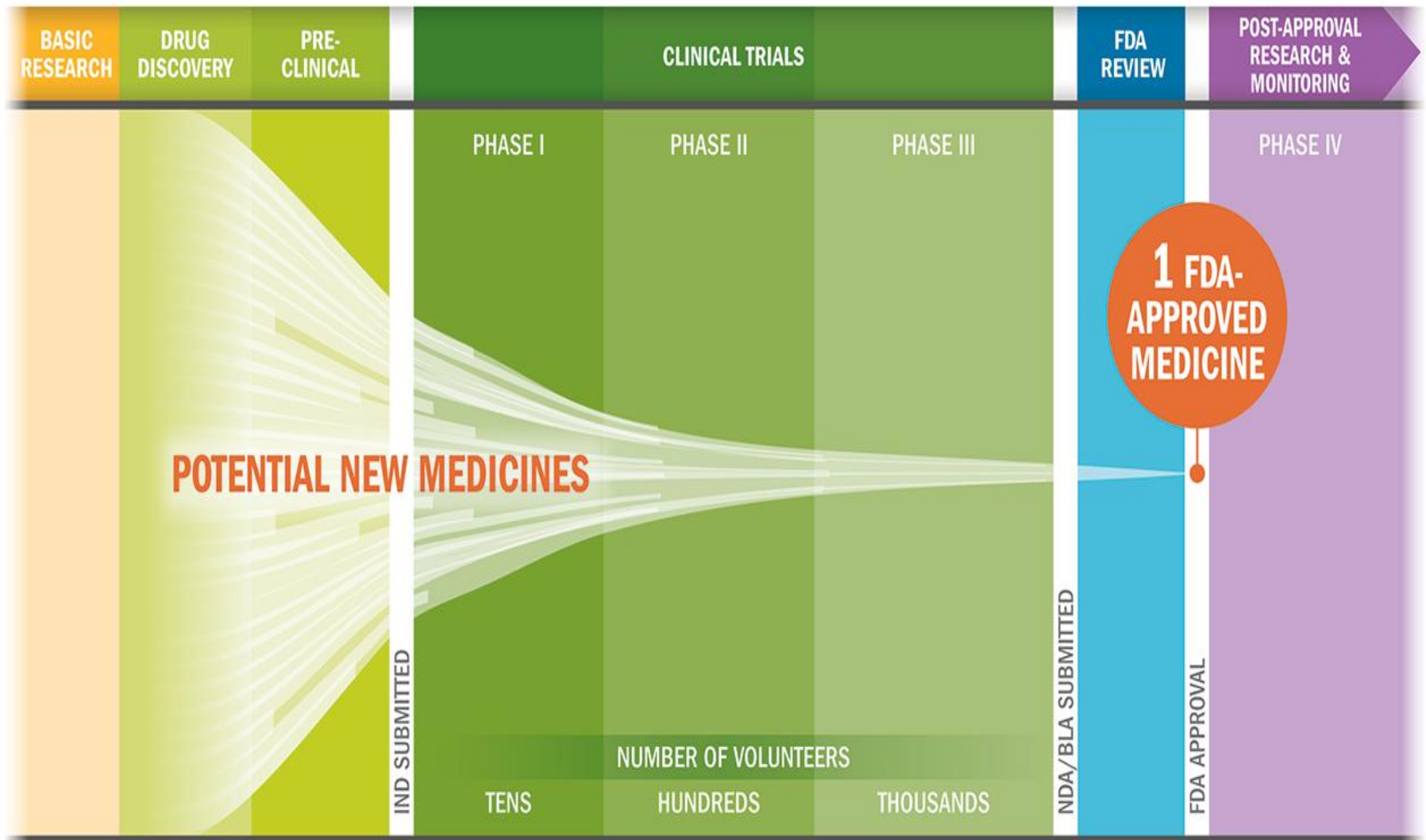


# Druggable Targets in SCD?

- Polymerization of sickle hemoglobin
- Alterations in RBC membrane
- Reduced nitric oxide bioavailability
- Endothelial dysfunction
- Platelet activation
- Pro-inflammatory cytokine production
- Activation of adhesion molecules on leukocytes, endothelial cells and platelets



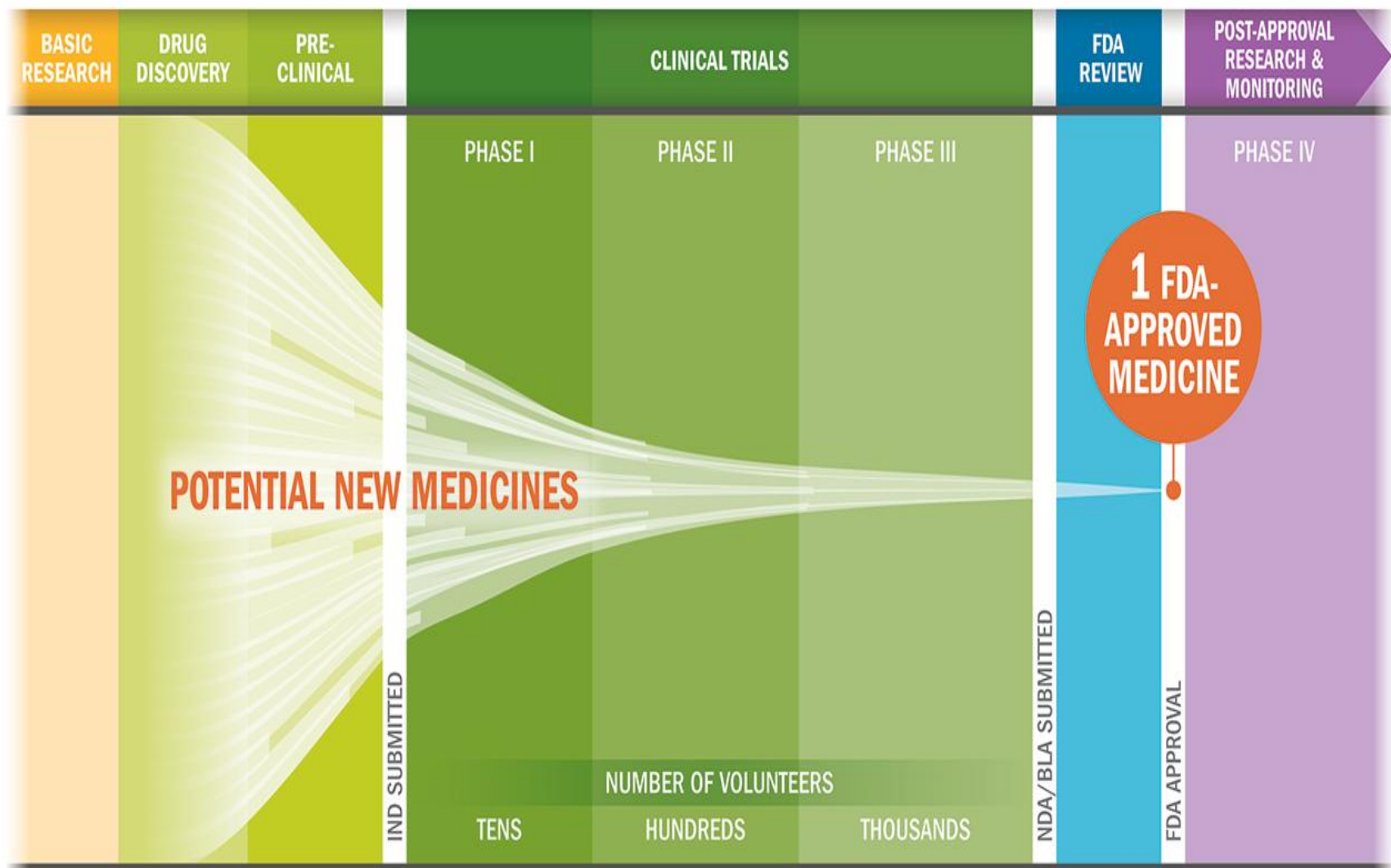
# The Biopharmaceutical Development Process



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

SOURCE: <http://chartpack.phrma.org/biopharma-chartpack/research-and-development/the-biopharmaceutical-research-and-development-process>

# ~\$2.6B over 10 years to bring therapy to market



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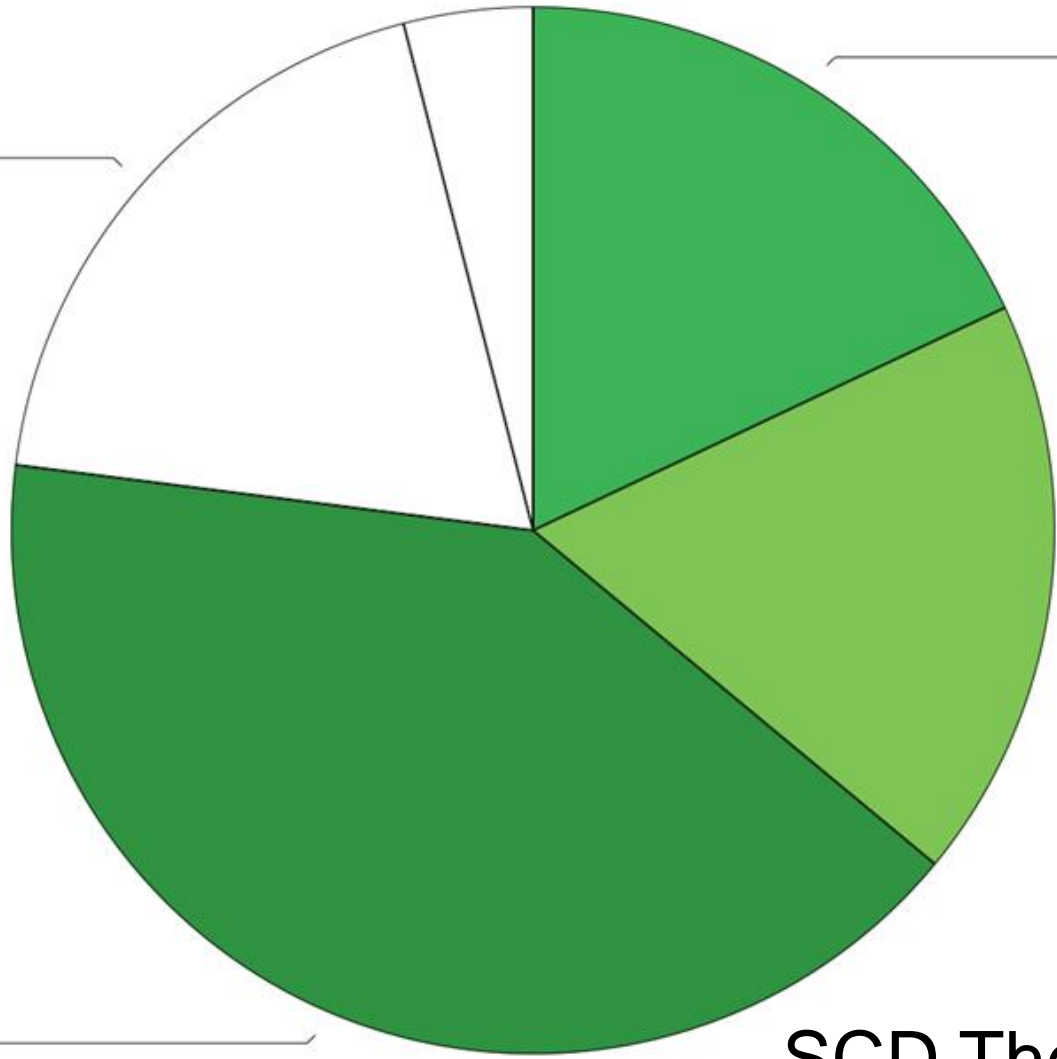
**Phase IV**  
4%

**Phase III**  
19%

**Phase II**  
41%

**Pre-Clinical**  
18%

**Phase I**  
18%



**SCD Therapeutics by  
Clinical Pipeline Phase**

# What this Means in Practice

There are going to be **many** more SCD-related clinical trials in the foreseeable future.

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They will all need patients from the same **limited** population.

# Exacerbating Existing Barriers

## 1. Finding appropriate investigators and sites

- Knowledgeable about the disease area
- Capacity for conducting clinical research

## 2. Finding eligible cohorts

- Sponsor's perspective: It is difficult to identify and recruit eligible patients
- Patient's perspective: It is difficult to identify trials for which I am eligible

## 3. Evaluating effectiveness

- Therapeutic outcome measures do not exist for many disease areas



# Moving Into An Era Of Novel Therapies for Sickle Cell Disease: Are We There Yet?

- Have we optimized use of existing treatment?
- How will the concomitant use of hydroxyurea affect the efficacy of new agents?
- Are we closer to having more therapeutic options for patients with sickle cell?