

Highlights from the 58th American Society of Hematology Annual Meeting

December 5, 2016



Agenda



Introduction

- Todd James, IRC
Senior Director, Investor Relations and Corporate Communications

MDS

- Steven Ertel
Chief Operating Officer

Myelofibrosis

- Matthew Sherman, M.D.
Chief Medical Officer

Beta-Thalassemia

- Matthew Sherman, M.D.
Chief Medical Officer

Question & Answer Session

Acceleron Forward-Looking Statements



This presentation contains forward-looking statements about Acceleron's strategy, future plans and prospects, including statements regarding the development of luspatercept and sotatercept, the timeline for clinical development and regulatory approval of Acceleron's compounds, the expected timing for the reporting of data from ongoing trials, and the structure of Acceleron's planned or pending clinical trials. The words "anticipate," "appear," "believe," "continue," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks that preclinical testing of Acceleron's compounds and data from clinical trials may not be predictive of the results or success of ongoing or later clinical trials, that data may not be available when Acceleron expects it to be, that Acceleron or its collaboration partner, Celgene, will be unable to successfully complete the clinical development of Acceleron's compounds, that the development of Acceleron's compounds will take longer or cost more than planned, that Acceleron or Celgene may be delayed in initiating or completing any clinical trials, that Acceleron's compounds will not receive regulatory approval or become commercially successful products.

Other risks and uncertainties include those identified under the heading "Risk Factors" included in Acceleron's Annual Report on Form 10-K which was filed with the Securities and Exchange Commission (SEC) on February 25, 2016, and other filings that Acceleron has made and may make with the SEC in the future. The forward-looking statements contained in this press release reflect Acceleron's current views with respect to future events, and Acceleron does not undertake and specifically disclaims any obligation to update any forward-looking statements.

Building a Blockbuster Hematology Brand with Celgene



A new approach to treating chronic anemias that is differentiated from all other agents

Phase 3

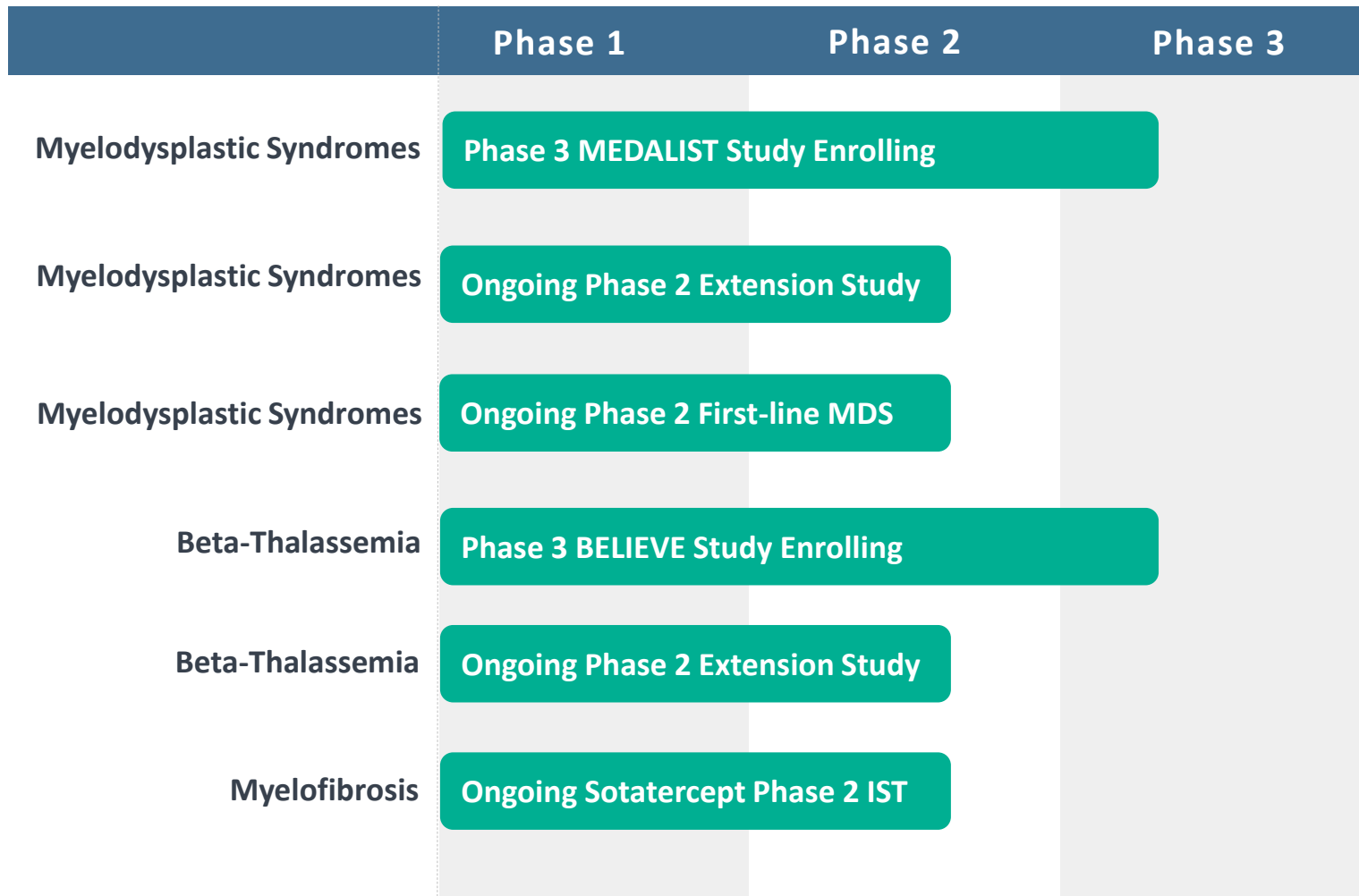


Phase 2*



*Indications in addition to current Phase 3 study indications

Robust Program of Multiple Phase 2 and Phase 3 Studies in Hematology



Luspatercept & Sotatercept Clinical Presentations

MDS

- Luspatercept Increases Hemoglobin and Reduces Transfusion Burden in Patients with Low-Intermediate Risk Myelodysplastic Syndromes (MDS): Long-Term Results from Phase 2 PACE-MDS Study
- Pharmacokinetics and Exposure–Response of Luspatercept in Patients with Anemia Due to Low- or Intermediate-1-Risk Myelodysplastic Syndromes

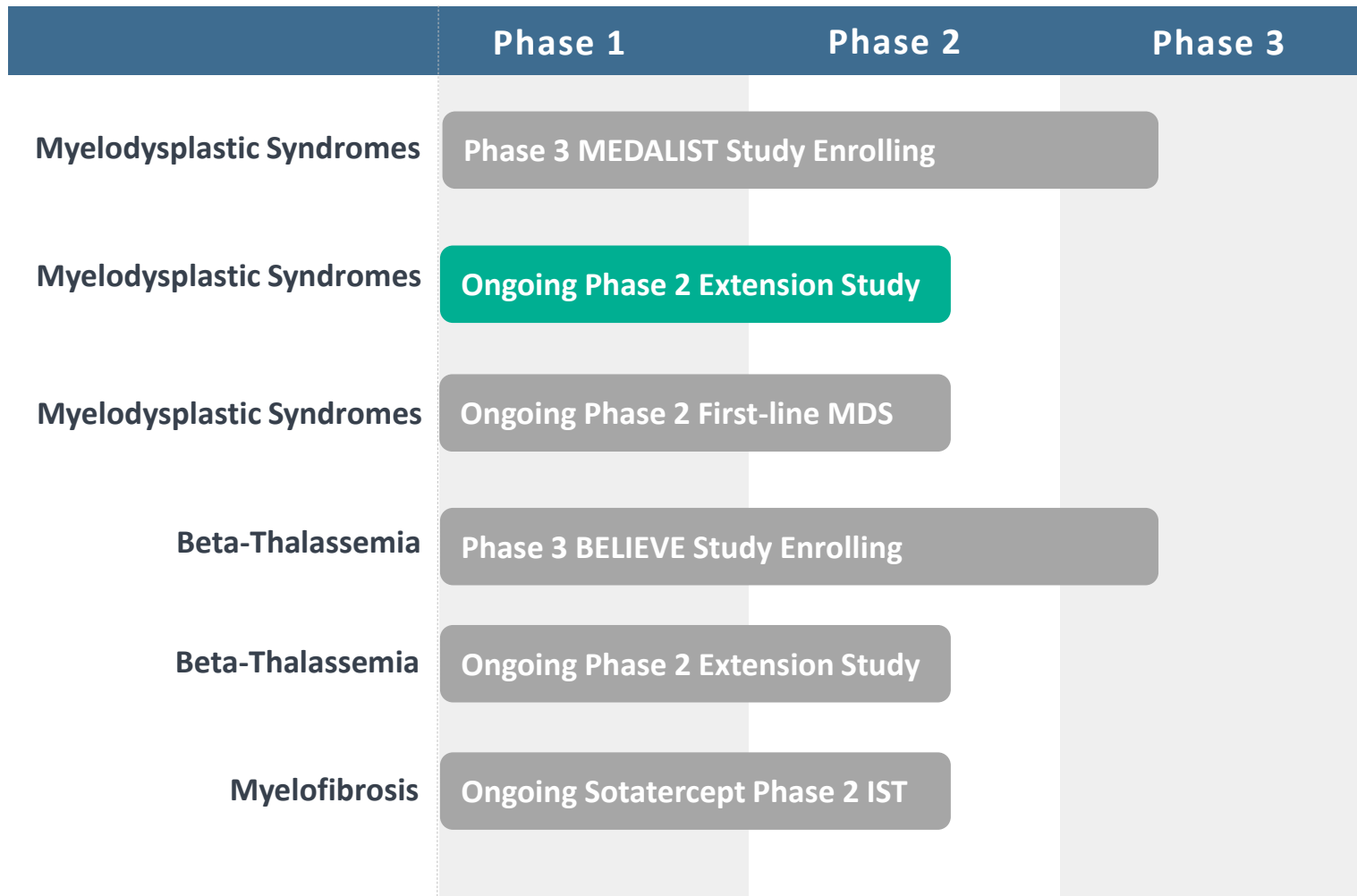
Beta-thalassemia

- Luspatercept Increases Hemoglobin, Decreases Transfusion Burden and Improves Iron Overload in Adults with Beta-Thalassemia
- Pharmacokinetics and Exposure–Response of Luspatercept in Patients with Beta-Thalassemia: Preliminary Results from Phase 2 Studies

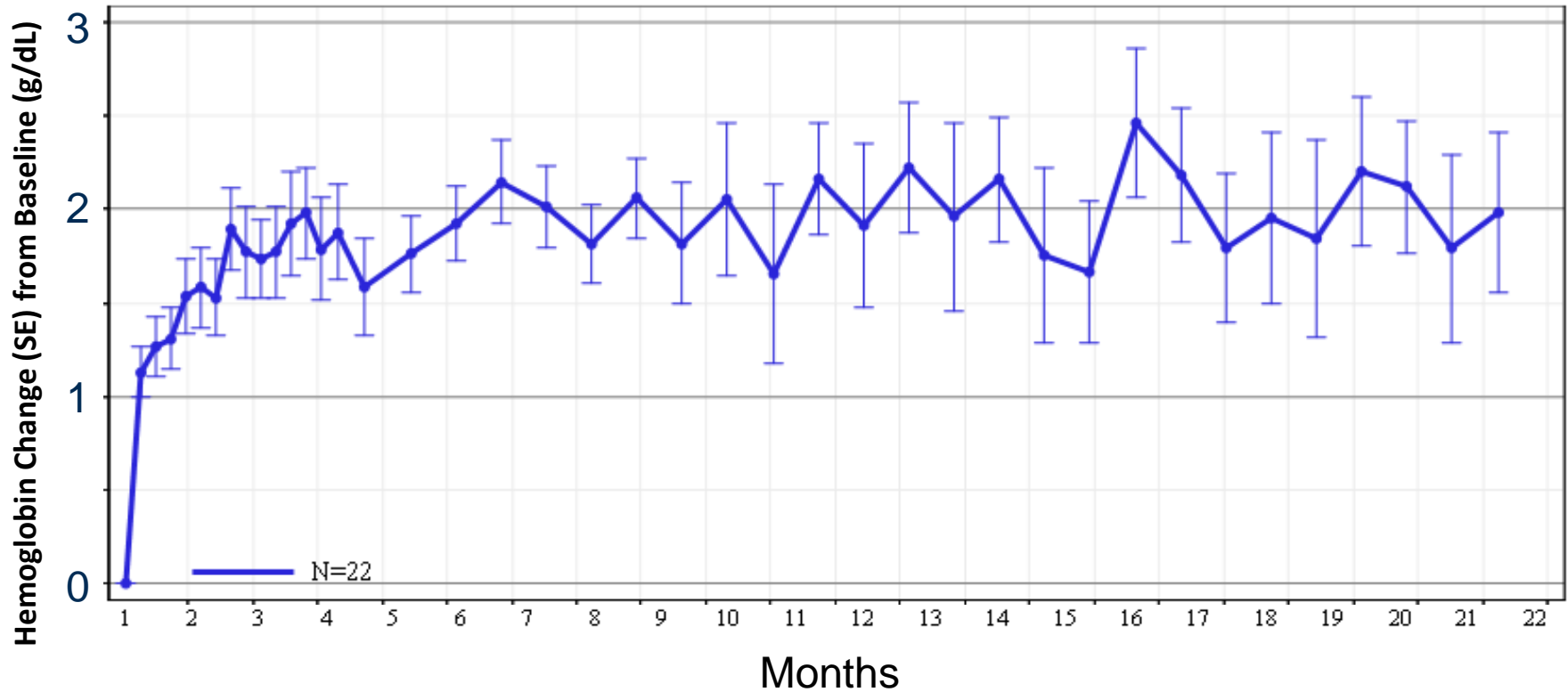
Myelofibrosis (Investigator Initiated Trial)

- Phase-2 Study of Sotatercept (ACE-011) in Myeloproliferative Neoplasm-Associated Myelofibrosis and Anemia

Robust Program of Multiple Phase 2 and Phase 3 Studies in Hematology



Increase in Mean Hemoglobin in LTB Patients with > 3 Months of Treatment (Extension Study)



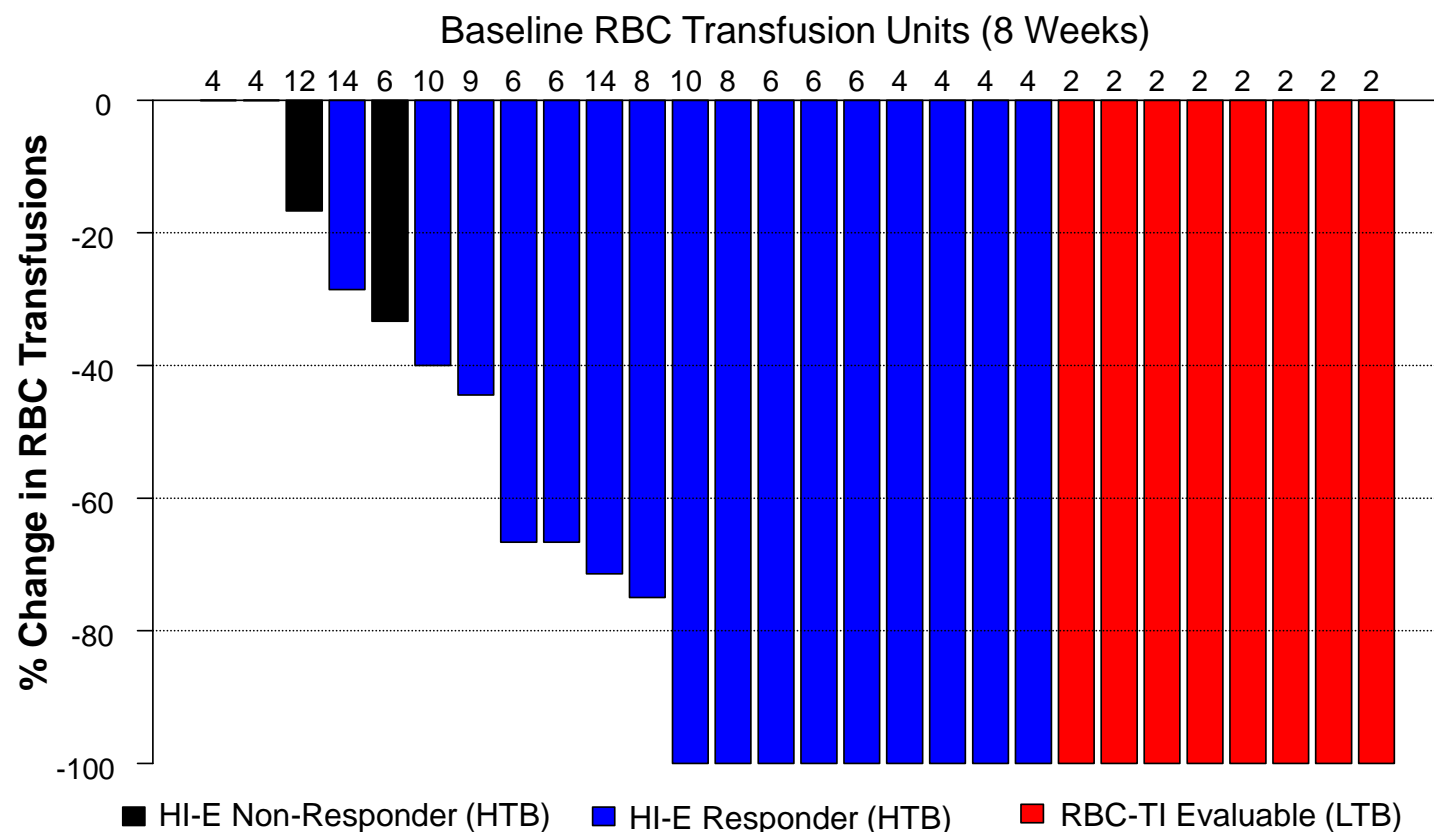
patients 22* + + + + + + + + + + + + + + + + 18 21 19 21 20 20 17 15 15 12 11 11 12 13 13 11 11 12 12 10 10 10 9 9 8 8 7 7

LTB: Low transfusion burden patients (< 4 units/8 wk, Hb <10 g/dL)

Reduction in Transfusion Burden in Patients with > 3 Months of Treatment (Extension Study, N=28)



- 61% (17/28) patients achieved RBC transfusion independence ≥ 8 weeks
- 80% (16/20) HTB patients were HI-E responders (≥ 4 unit decrease /8 weeks)



LTB: Low transfusion burden patients (< 4 units/8 wk, Hb <10 g/dL)

HTB: High transfusion burden patients (≥ 4 units/8 wk)

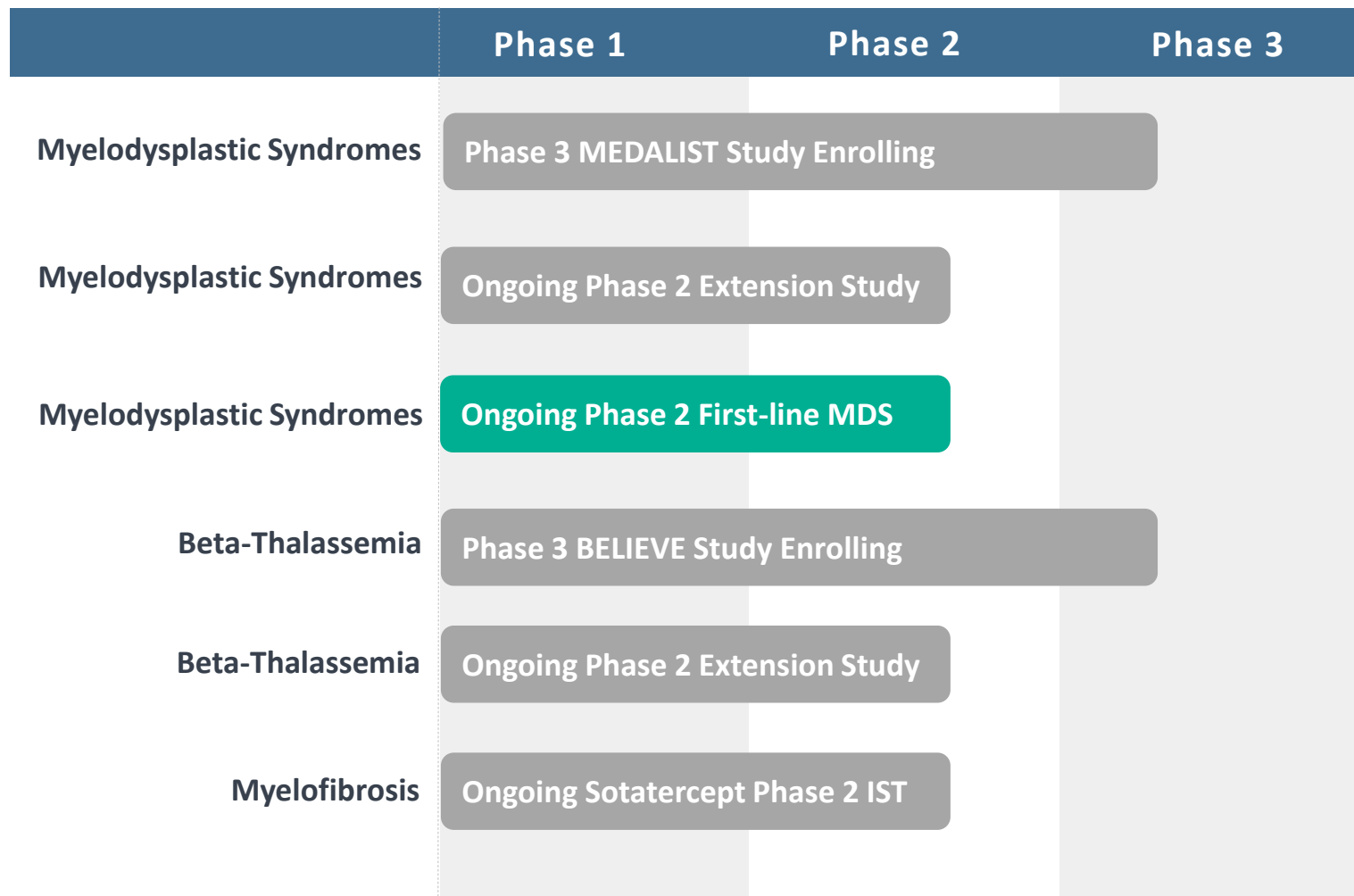
HI-E Response and TI by Baseline EPO and RS Status

Patients Treated at Doses ≥ 0.75 mg/kg

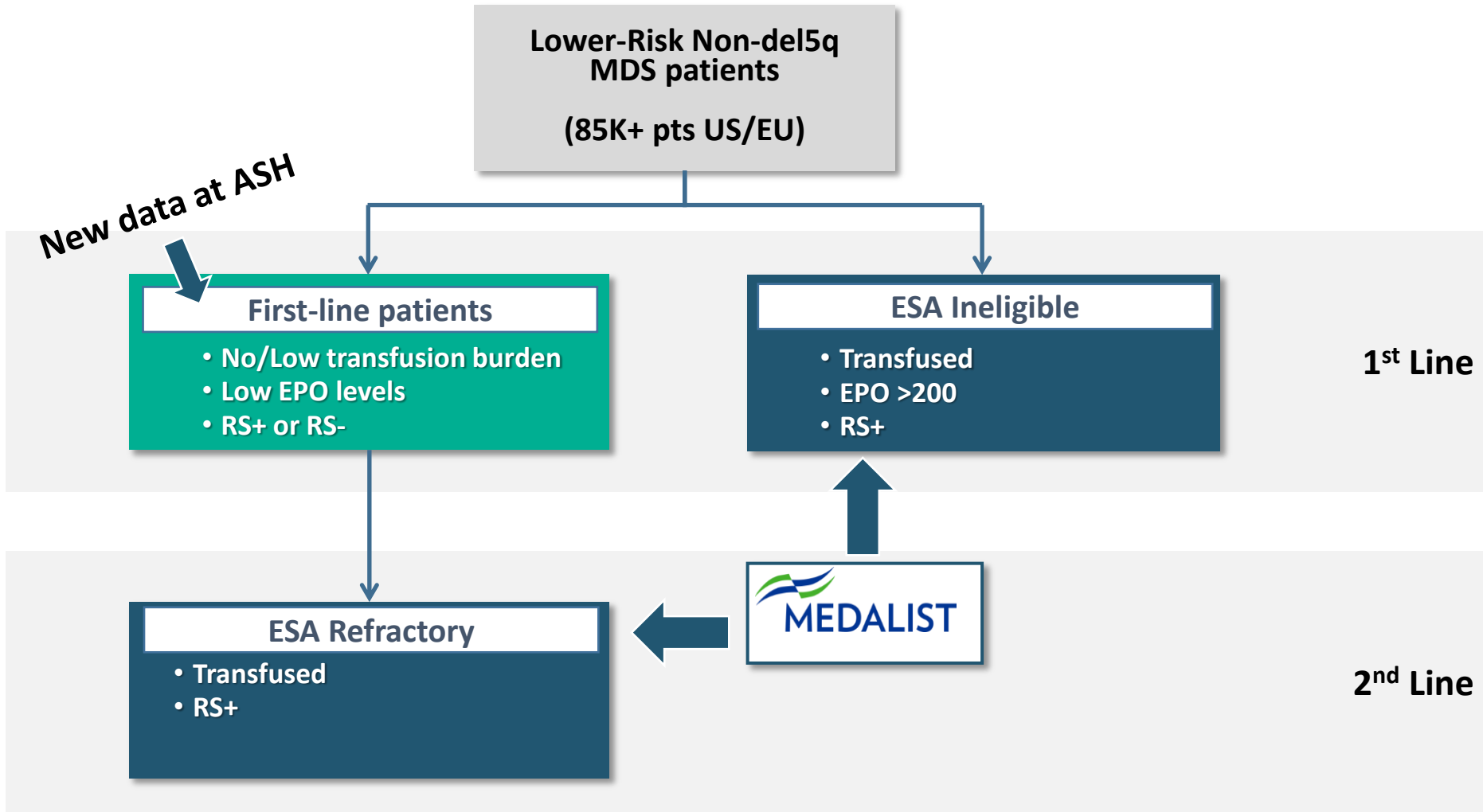


Baseline EPO (U/L)	RS Status	<u>IWG HI-E, n/N (%)</u>		<u>RBC-TI, n/N (%)</u>	
		Base	Extension	Base	Extension
< 200	RS+	18/29 (62%)	19/23 (83%)	13/19 (68%)	10/14 (71%)
	RS-	2/5 (40%)	3/3 (100%)	1/4 (25%)	1/2 (50%)
≥ 200 to ≤ 500	RS+	5/11 (46%)	7/8 (88%)	3/9 (33%)	3/5 (60%)
	RS-	0/3 (0%)	0/1 (0%)	2/2 (100%)	1/1 (100%)

Robust Program of Multiple Phase 2 and Phase 3 Studies in Hematology



Luspatercept MDS Population in Ongoing Phase 2 and Phase 3 Studies



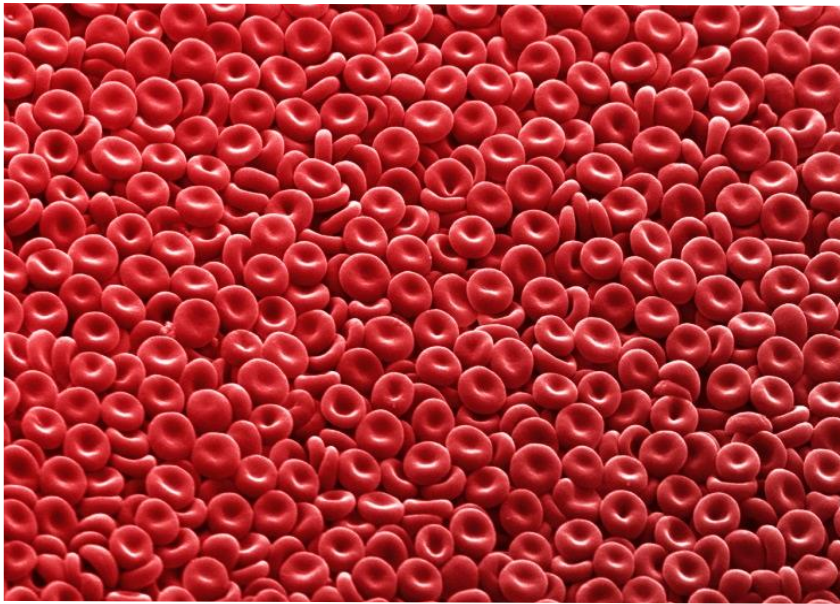
Patient Response Rates in ESA Naïve and EPO < 500 Subpopulations

Patients Treated at Doses ≥ 0.75 mg/kg



IWG HI-E, n/N (%)		RBC-TI, n/N (%)	
3-months Treatment	> 3-months Treatment	3-months Treatment	> 3-months Treatment
12/20 (60%)	13/16 (81%)	9/12 (75%)	8/10 (80%)

Myelofibrosis



Myelofibrosis: Disease Overview



DISEASE

- Scarred, fibrotic bone marrow results in multiple cytopenias
- Patients suffer from severe anemia
- 30% present at diagnosis and eventually majority develop anemia

PREVALENCE

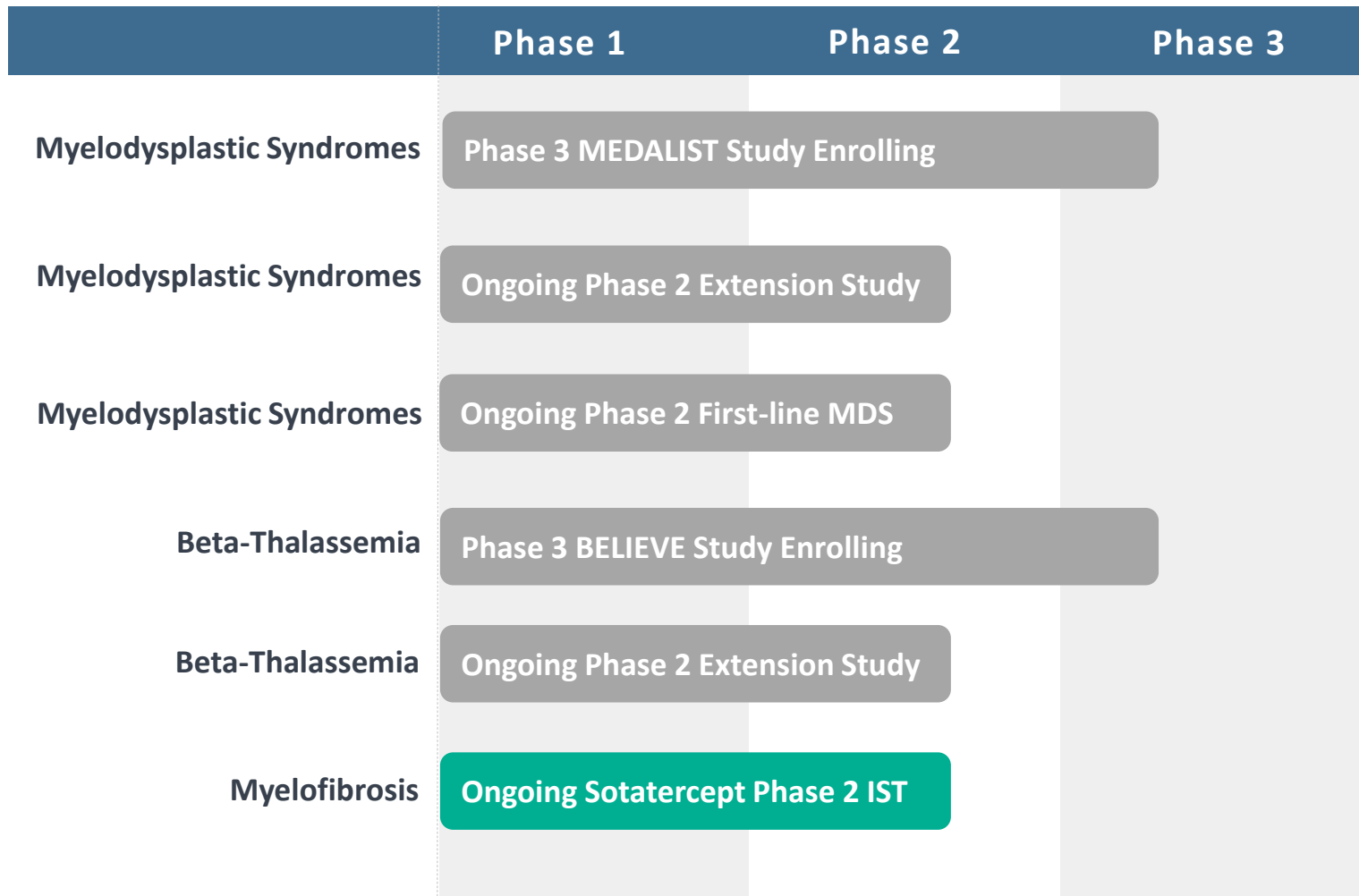
- Estimated 30,000 to 40,000 patients in the US and EU

CURRENT TREATMENTS

- No approved therapy for anemia in MF: RBC transfusions, ESAs, and IMiDs
- Ruxolitinib for enlarged spleen and symptom reduction
 - Anemia is not improved, and initially worsened by ruxolitinib

Therapeutic Goal in Myelofibrosis: Correct Anemia and Eliminate/Reduce RBC Transfusions

Robust Program of Multiple Phase 2 and Phase 3 Studies in Hematology



Sotatercept MD Anderson Phase 2 IIT Design in MF



- **Adults with Primary MF (PMF) or Post Polycythemia Vera (PV)/ Essential Thrombocythemia (ET) MF who are either:**
 - RBC transfusion-dependent or,
 - consistently have hemoglobin (Hgb) <10 g/dl over ≥ 12 weeks, or
 - have Hgb <10 g/dl with sporadic transfusions
- **3 patient cohorts of up to 20 patients each**
 - sotatercept 0.75 mg/kg and 1.0 mg/kg cohorts
 - sotatercept in combination with ruxolitinib cohort
- **Response criteria**
 - Anemia response = composite of Hgb response and RBC transfusion independence (defined per IWG-MRT criteria)
 - Hgb response: Hgb increase of ≥ 1.5 g/dl on every determination consecutively over ≥ 12 wks without RBC transfusions
 - Subjects must have received ≥ 5 cycles to be evaluable for response

Results: Efficacy in MF



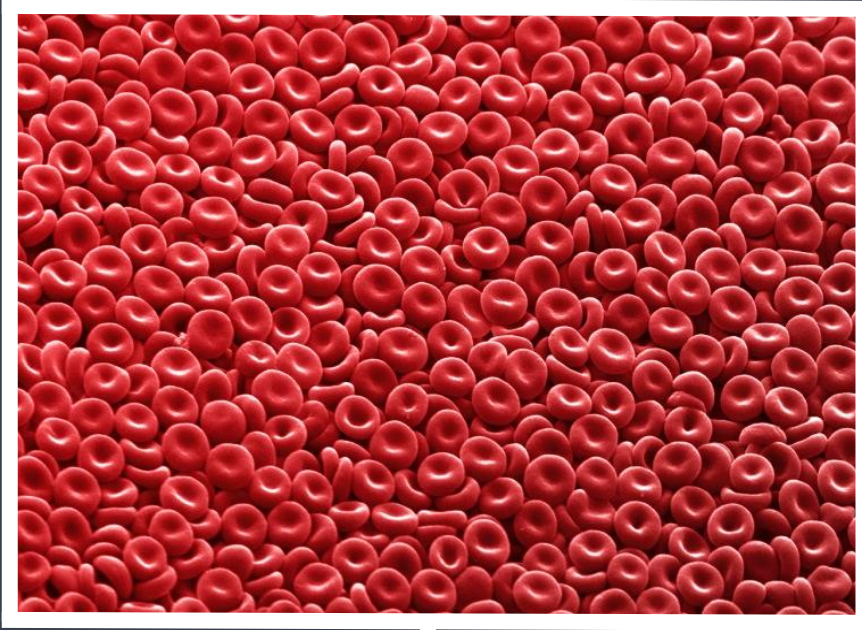
- 5 of 14 (36%) evaluable patients have responded

Responses by category		
Dose	0.75 mg/kg	4 of 10 (40%)
	1 mg/kg	1 of 4 (25%)
Transfusion dependence	Dependent (IWG)	3 of 10 (33%)
	Independent	2 of 4 (50%)

Sotatercept Summary



- Sotatercept well-tolerated and active in anemia of MF
- Celgene and Acceleron considering company sponsored trial in MF
- Studies with sotatercept in chronic kidney disease have been deprioritized



Luspatercept in Beta-thalassemia

Beta-Thalassemia: Disease Overview



DISEASE

- Debilitating inherited hematologic disease of defective red blood production
- Patients suffer from severe anemia and multiple organ dysfunction from excess iron deposits

PREVALENCE

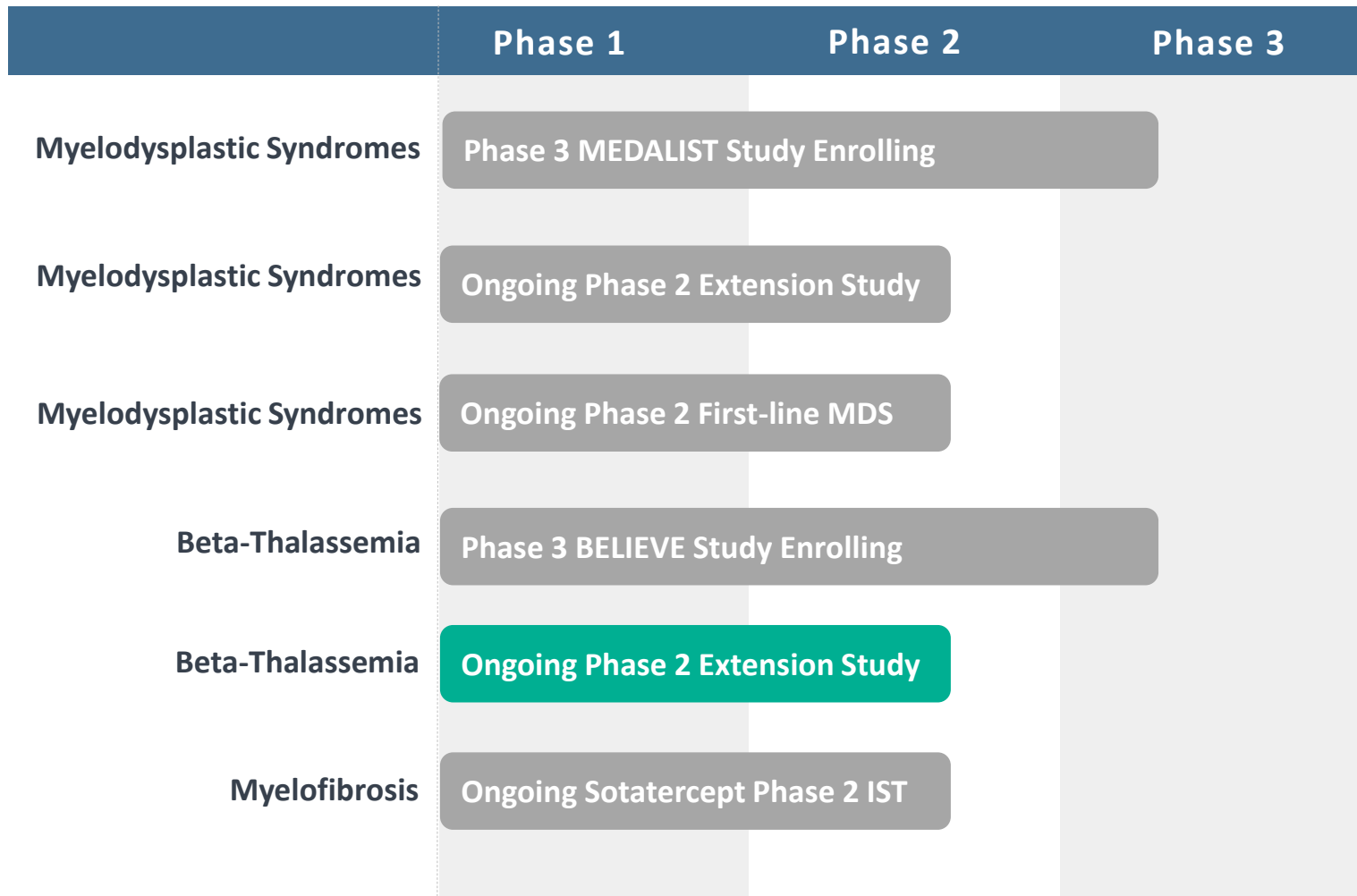
- Estimated 40,000 patients in the US and EU
- \approx 300,000 transfusion-dependent patients globally

CURRENT TREATMENTS

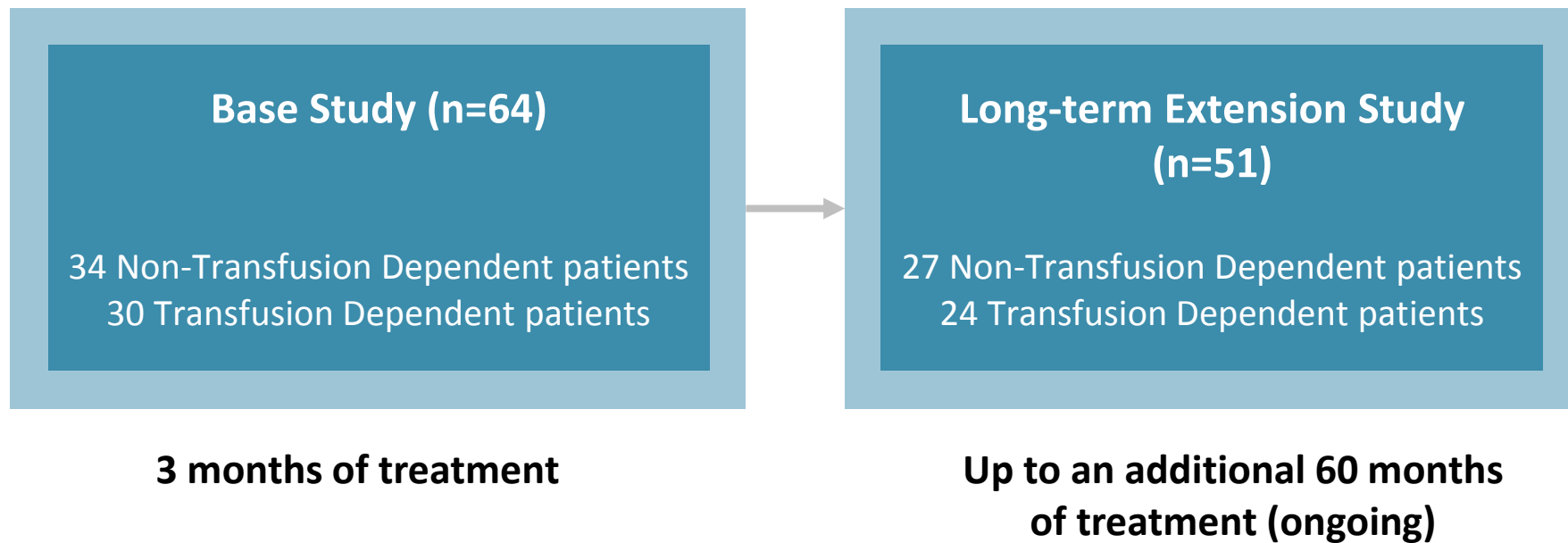
- Red blood cell transfusions (RBC), iron chelation therapy, hematopoietic stem cell transplant
- RBC transfusions increase risk of viral transmission, iron overload and other disease complications

Therapeutic Goal in Beta-Thalassemia: Reduce RBC Transfusions

Robust Program of Multiple Phase 2 and Phase 3 Studies in Hematology



Luspatercept Beta-thalassemia Phase 2 Studies



- Luspatercept increases hemoglobin and achieves durable transfusion independence in patients with lower risk myelodysplastic syndromes
- Preliminary data in ESA naïve and RS- (EPO < 200) MDS patients are encouraging
- Luspatercept generates sustained increases in hemoglobin levels, reduced transfusion burden, and improved patient reported quality of life measures in patients with beta-thalassemia
- Preliminary results show that treatment with investigational drug sotatercept can increase hemoglobin and achieve transfusion independence in patients with myelofibrosis
- Data at ASH highlights potential for these molecules to treat an increasingly large and expanding set of hematologic diseases, including MDS, beta-thalassemia, and now myelofibrosis

Building a Blockbuster Hematology Brand with Celgene



A new approach to treating chronic anemias that is differentiated from all other agents

Phase 3



Phase 2*



*Indications in addition to current Phase 3 study indications

ASH 2016 Q&A Session



Steven Ertel

Chief Operating Officer

Matthew Sherman, M.D.

Chief Medical Officer

Todd James, IRC

Investor Relations and Corp. Comm.

