SILENCE THERAPEUTICS

SANRECO Phase 2 Topline Results in Polycythemia Vera

August 10, 2026

Forward-Looking Statements

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Introduction

Iain Ross, Chairman and Interim Principal Executive Officer

Silence – siRNA Platform Company with Compelling Clinical Data Across Multiple Programs

GOLD PLATFORM

- Proven GalNAc siRNA technology with broad utility
- Potent, durable and highly specific gene silencing
- Infrequent dosing enabled by durable pharmacology
- Strong and growing IP portfolio

CLINICAL RESULTS

- Four clinical-stage assets targeting large unmet needs in rare and cardiometabolic diseases
- Compelling clinical data generated across multiple programs

FRANCHISE OPPORTUNITY

- Divesiran: first-in-class siRNA for PV
- ~150K U.S. / ~3.5M global PV population[1]
- Potential best-in-class profile
- Additional pipeline opportunities beyond PV

1. Using 44/100,000 global population: 7,800m, Kattamis, A. et al. Eur J Haematol (2020)

PV: Large Unmet Need and Proven Market Value Create Significant Upside for a Best-in-Class Therapy

Large Underserved Population [2-5]

- Many PV patients remain phlebotomy-dependent
- Persistent burden reflects inadequate control
- Broad addressable population needs better therapy

Current Options are Limited [2-5]

- Limitations in efficacy, safety and tolerability
- Chronic treatment burden and poor experience
- Jakafi generates ~$1B annually in PV despite later-line label limitations and treatment tradeoffs[1]

Compelling Product Profile

- Robust efficacy
- Favorable safety
- Infrequent dosing
- Better patient experience

A best-in-class PV therapy could unlock blockbuster potential in a large underserved market

1. According to Incyte financial disclosures and market share data 2. Verstovsek S, et al. Ann Hematol. 2023 Mar;102(3):571-581; 3. Verstovsek S, et al. Leuk Res. 2017;56:5259.doi:10.1016/j.leukres.2017.01.032.; 4. McMullin MF, et. al. Br J Haematol. 2019 Jan; 184(2): 176-191.; 5. Mesa, R. Clin Adv Hematol Oncol (2017)

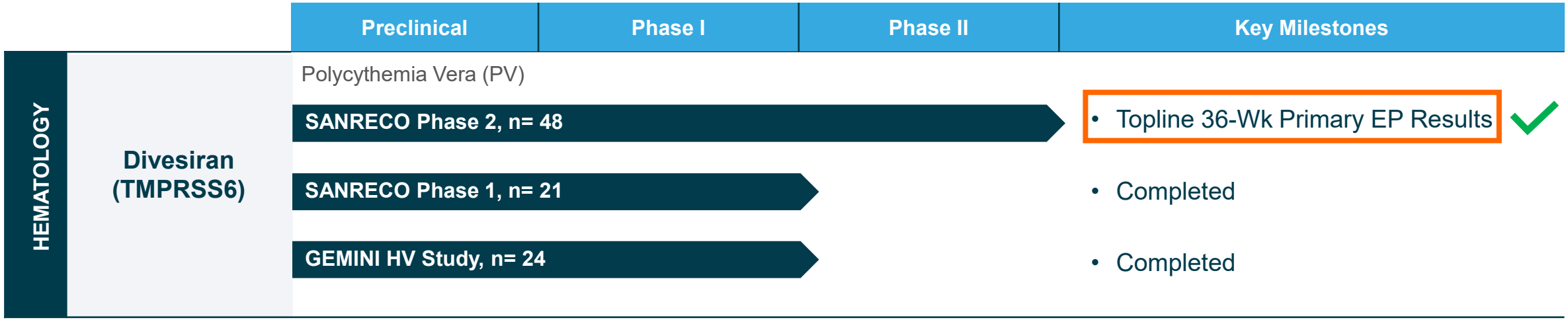
SANRECO Results Support Potential Best-in-Class Treatment for Phlebotomy-Dependent PV Patients

SANRECO Phase 2 Topline Results

Steven Romano, MD, Chief R&D Officer

Divesiran Clinical Development Program
Polycythemia Vera

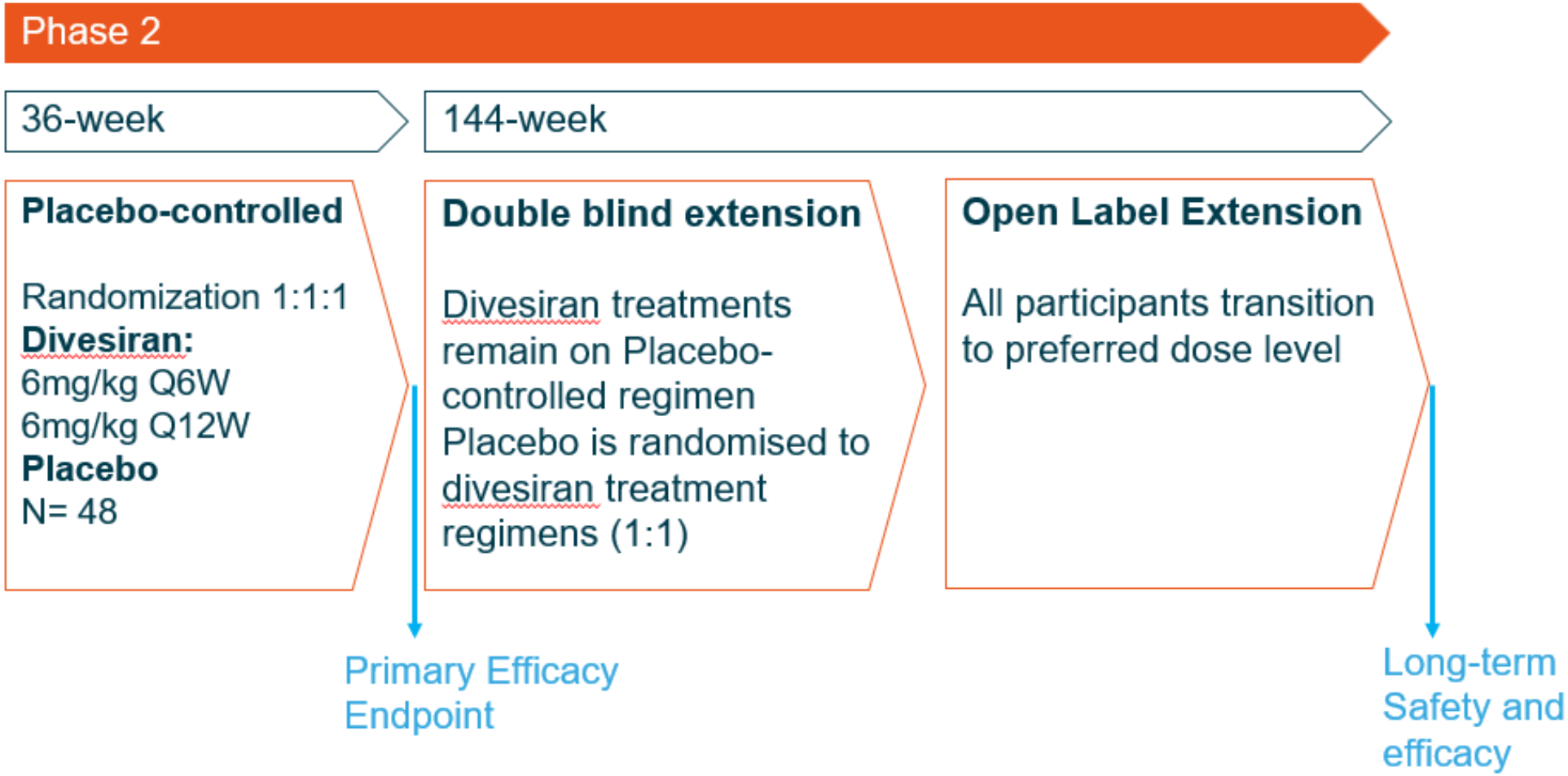
- PV is a rare myeloproliferative neoplasm characterized by excessive production of red blood cells
  - Elevated hematocrit (Hct) >45%
  - Primary treatment goal is to maintain Hct <45%



Divesiran has orphan drug and fast track status in PV

Phase 2 SANRECO Study is a Global Trial: 9 Countries / 4 Continents

Phase 2 SANRECO Study: Clinical Study Design



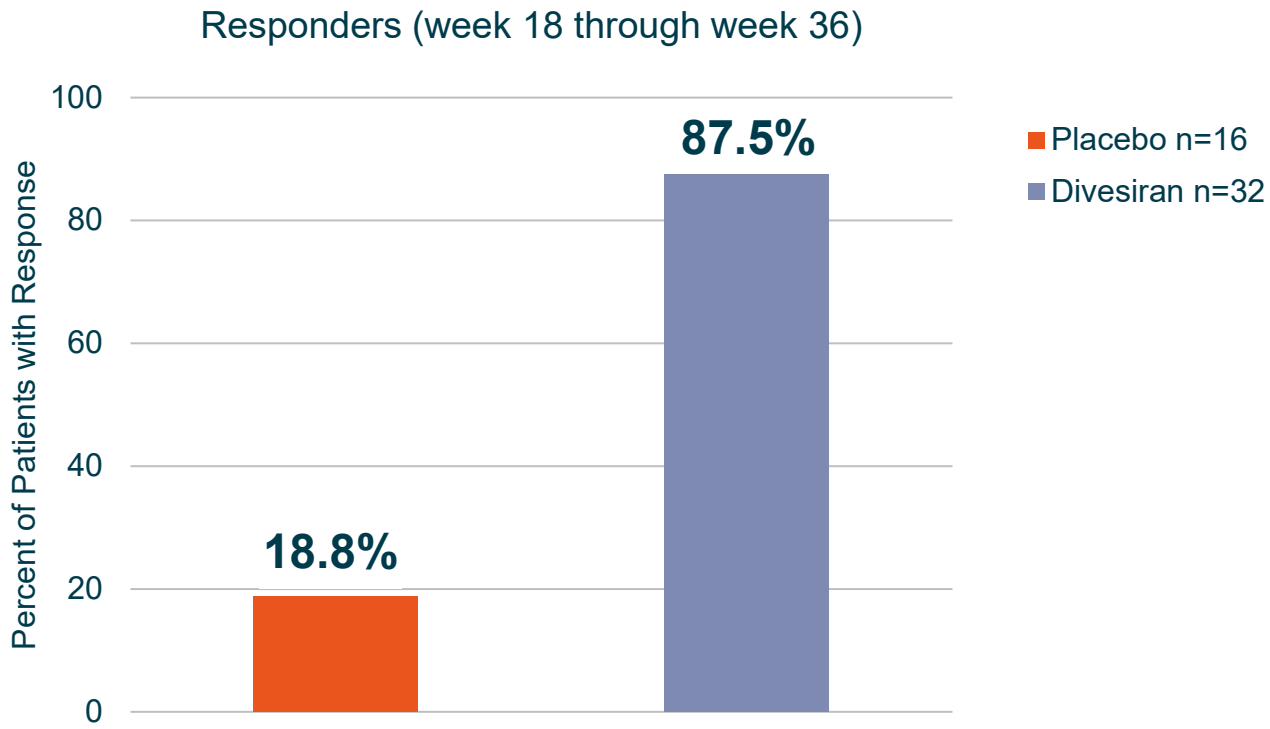
SANRECO Phase 2 Study Overview

Design	• 36-week, placebo-controlled, double-blind period followed by a 3-year, double-blind and open-label extension period evaluating divesiran in 48 phlebotomy-dependent PV patients
Key Inclusion Criteria	• PV diagnosis • At least 3 phlebotomies in the last 6 months or 5 in the last year prior to screening • Stable dose of cytoreductive agents allowed • HCT level <45% prior to dosing
Dosing & Administration	• Divesiran 6 mg vs. placebo • Administered s.c. at Q6W and Q12W intervals
Key Objectives	• Primary endpoint: proportion of patients who maintain HCT levels below 45% without phlebotomies between weeks 18 and 36 • Secondary endpoints include safety and tolerability, pharmacokinetics, and quality of life changes

SANRECO: Primary Efficacy Endpoint - Response Rate

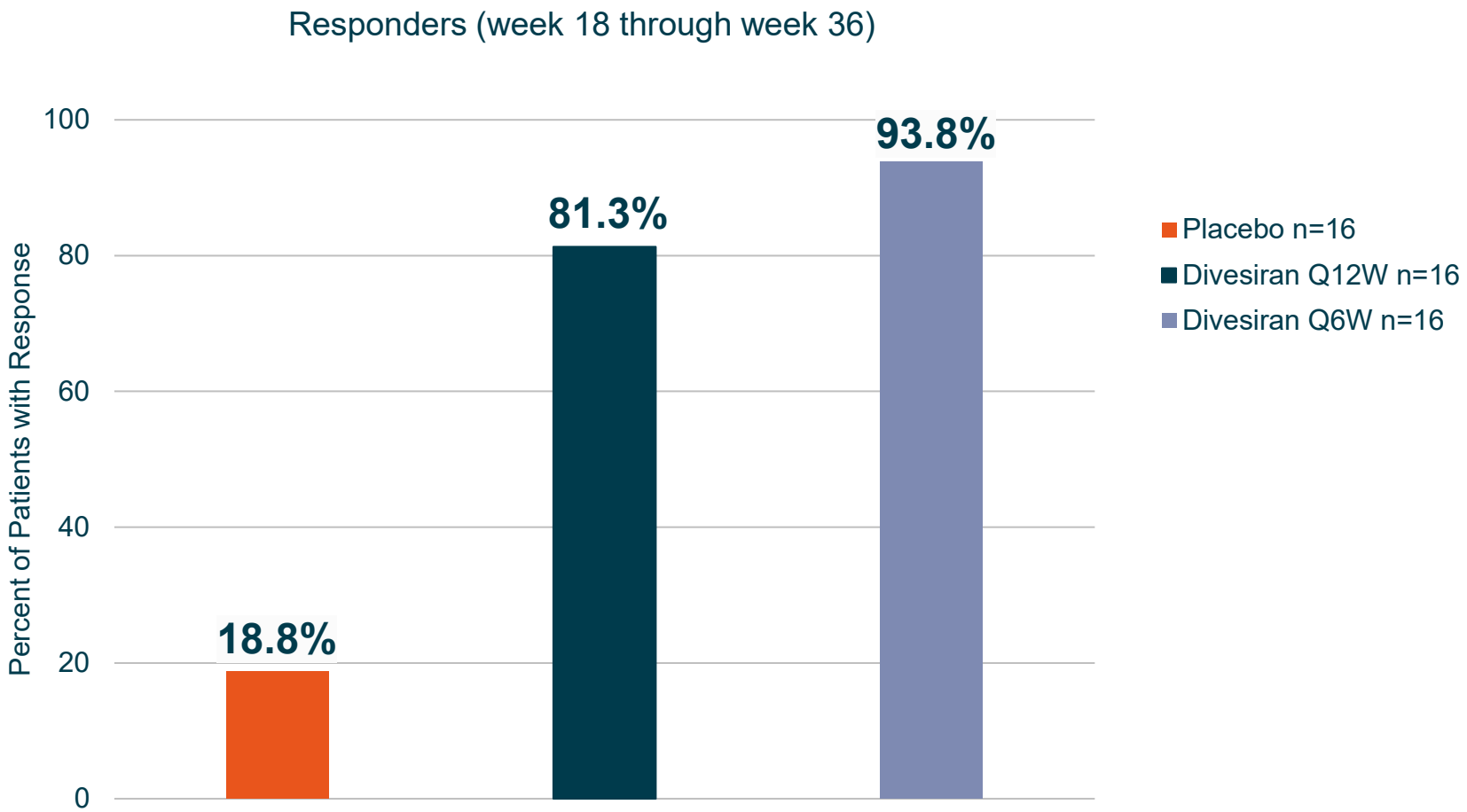
The **primary endpoint was met:**

- Significantly higher proportion of clinical responders among the divesiran treated PV patients **(88%)** compared to those who received placebo **(19%)** during weeks 18-36; p<0.0001
- **Placebo adjusted response rate = 69%**



Note: Response is defined as HCT remaining below 45% and no phlebotomies received during weeks (18-36)

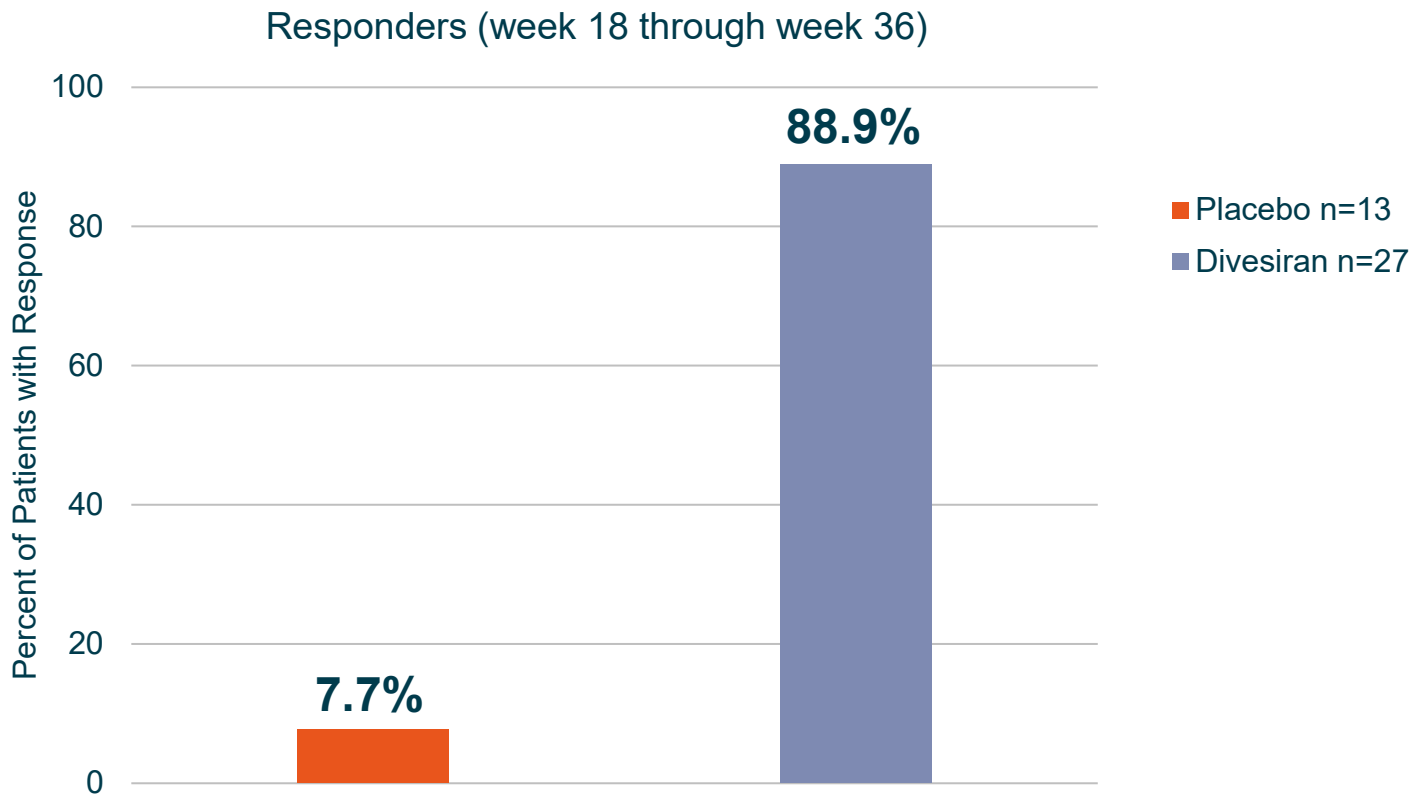
SANRECO: Primary Efficacy Endpoint by Dose Groups



Note: Response is defined as HCT remaining below 45% and no phlebotomies received during weeks 18-36

SANRECO: Response Rate Sensitivity Analysis (n=40)*

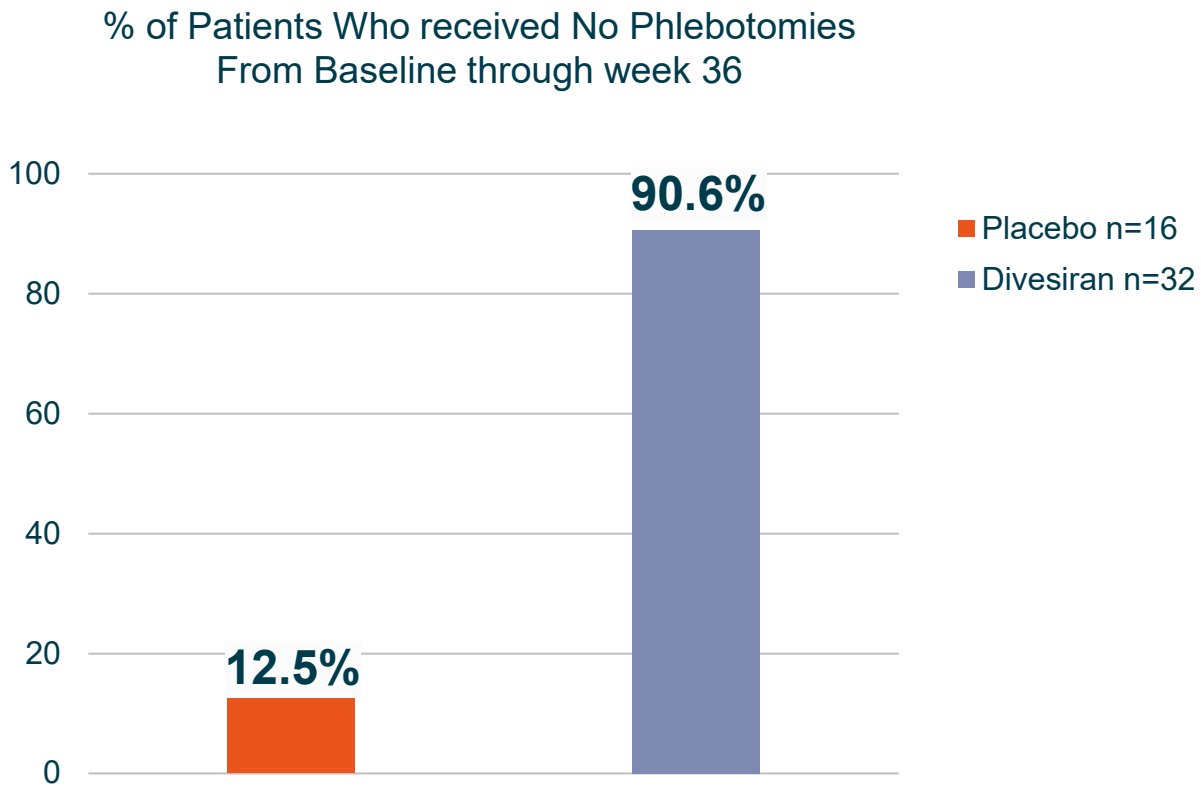
- Significantly higher proportion of clinical responders among the divesiran treated PV patients **(89%)** compared to those who received placebo **(8%)** during weeks 18-36; p<0.0001
- **Placebo adjusted response rate = 81%**



Note: Response is defined as HCT remaining below 45% and no phlebotomies received during weeks 18-36
*All patients who met the Phase 1 criterion of a minimum of 3 phlebotomies in the previous 3 months or 5 in the previous 12 months

SANRECO: Key Secondary Endpoint - Phlebotomy Rate

- Mean number of phlebotomies in the divesiran arm was **0.2** compared to **2.1** phlebotomies in the placebo arm during weeks 0-36 ($p<0.0001$)



SANRECO: Other Secondary Endpoints

- Divesiran groups also showed improvements in:
  - Hematocrit control
  - Iron markers, including ferritin
  - Patient reported outcomes using MPN-SAF Total Symptom Score (MPN-SAF TSS)

Summary of Adverse Events (Weeks 0-36)

- Divesiran was generally well tolerated
- Safety profile was in line with previous divesiran trials; no new safety findings
- Injection site reactions were infrequent and self-limiting
- There were two investigator reported grade 1 anemia adverse event cases

Next Steps

- Phase 2 SANRECO full results
  – Submitted abstract to ASH Congress (Dec 12-15, New Orleans)
- End of Phase 2 meeting by year end
- Initiate Phase 3 study in 1H 2027

SANRECO Results Support Potential Best-in-Class Treatment for Phlebotomy-Dependent PV Patients

Efficacy Endpoints

– Primary endpoint was met at both Q6W and Q12W intervals

Safety Endpoints

– Well tolerated with no new safety findings

Infrequent Dosing

– Comparable efficacy and safety results across Q6W and Q12W intervals

Phase 2 profile supports potential best-in-class positioning in phlebotomy-dependent PV

Q&A

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THANK YOU!