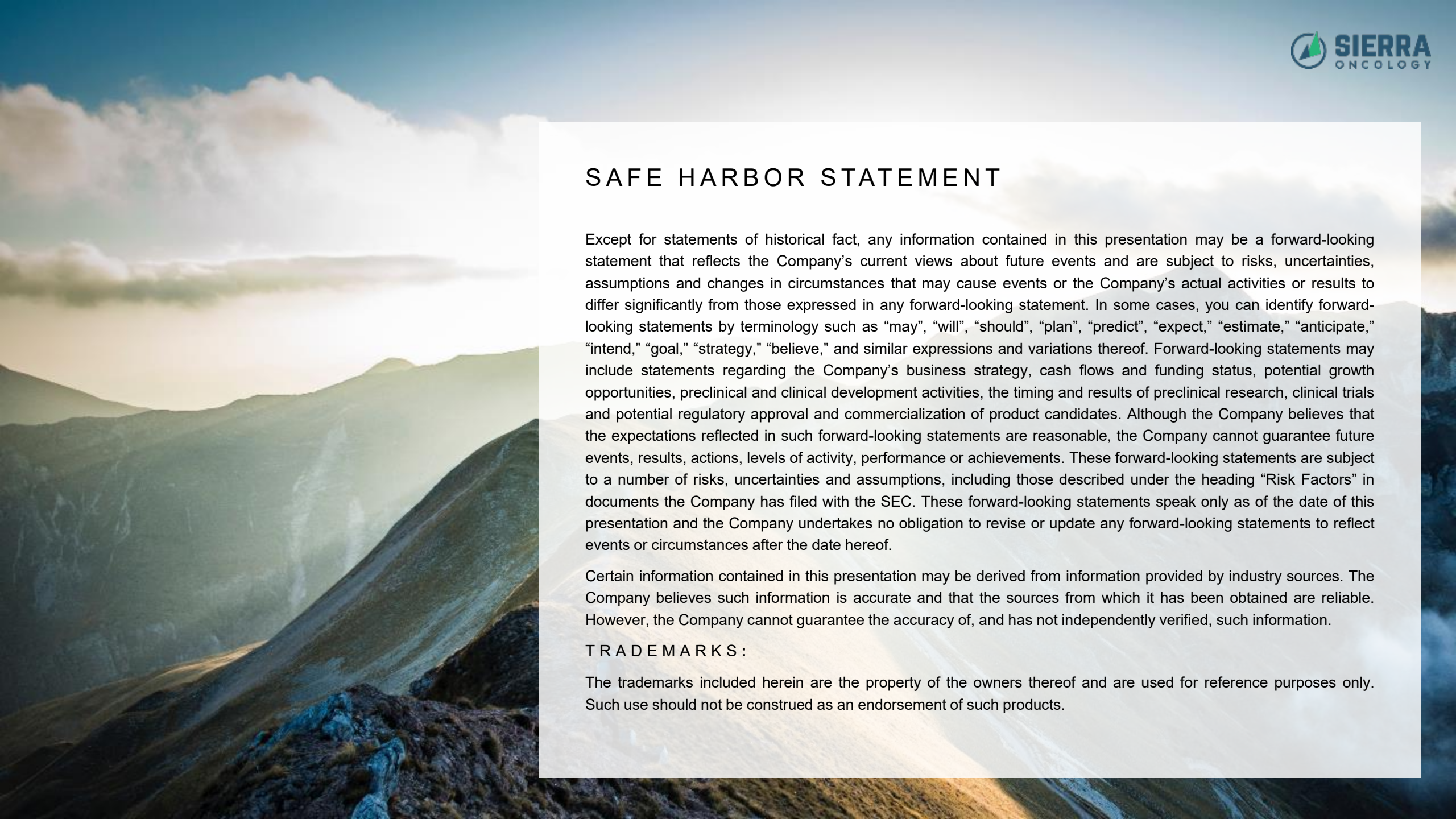
SIERRA ONCOLOGY

Building Momentum for Patients with Myelofibrosis

Q1 2020

NASDAQ: SRRA



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MOMELOTINIB

Positioned to potentially provide benefits on all three myelofibrosis hallmarks: symptoms, anemia and spleen

>20 studies
Phase 1, 2 and 3

>1,200 people
dosed with momelotinib

>820 patients
with myelofibrosis treated

>8 years
on treatment for several patients

Myelofibrosis
The Challenge of Anemia

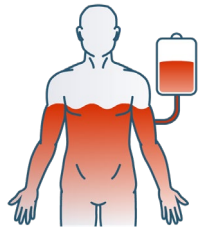
*"Anemia is major area of unmet need…
a quarter of the patients at the beginning may require transfusions, and after one year of therapy almost half of the patients already require transfusion"*

Srdan Verstovsek, MD, PhD
Professor in the Department of Leukemia at
The University of Texas MD Anderson Cancer Center, Houston

Unmet Medical Needs In Myelofibrosis; company conference call October 2018

Three Hallmarks of a Progressive Disease

64%



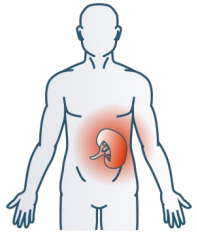
ANEMIA

Bone marrow cancer that significantly impairs red blood cell production

45% Transfusion Dependent

Many patients need regular blood transfusions to sustain life

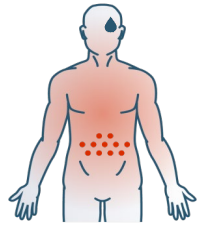
46%



SPLENOMEGALY

Spleen tries to compensate by making blood cells, leading to pain and discomfort

34%

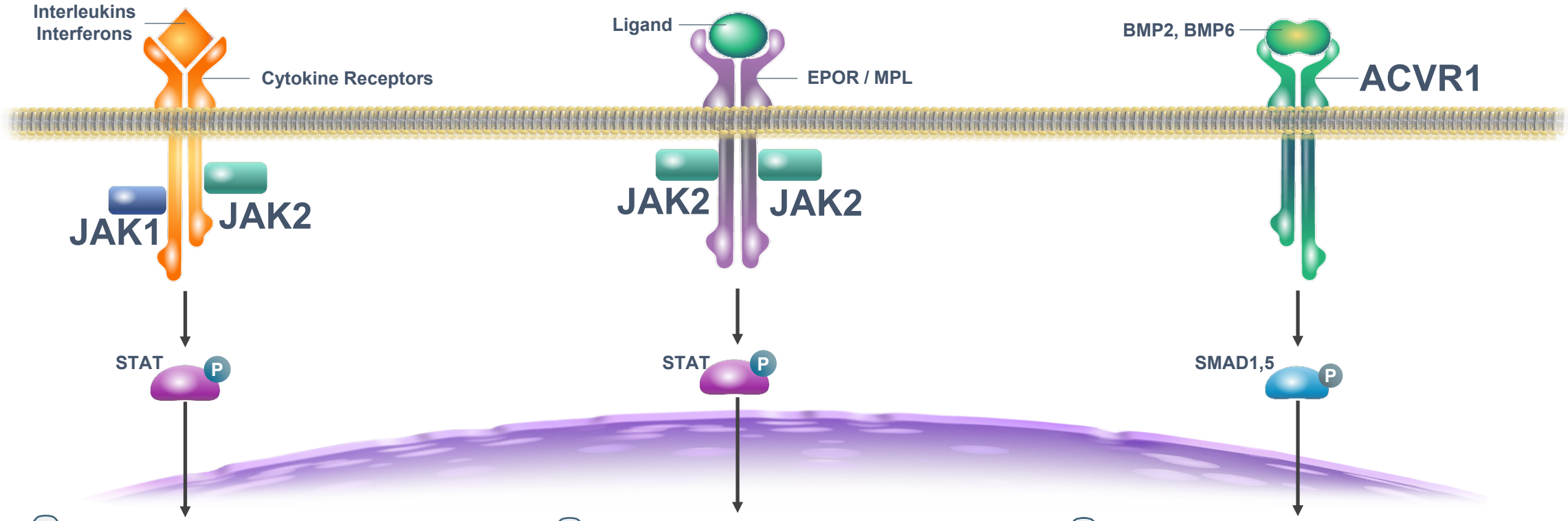


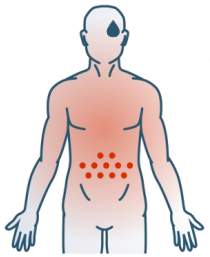
CONSTITUTIONAL SYMPTOMS

Patients also experience debilitating symptoms that dramatically impact their lives

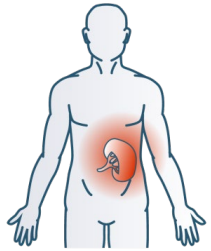
>1 year after diagnosis; Tefferi A, et al. *Mayo Clin Proc.* 2012

Myelofibrosis Biology:
JAK1, JAK2 & ACVR1 Drive Myelofibrosis Disease Hallmarks

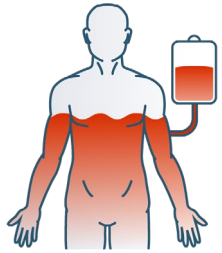




- Inflammation and aberrant cytokine signaling producing debilitating **constitutional symptoms**

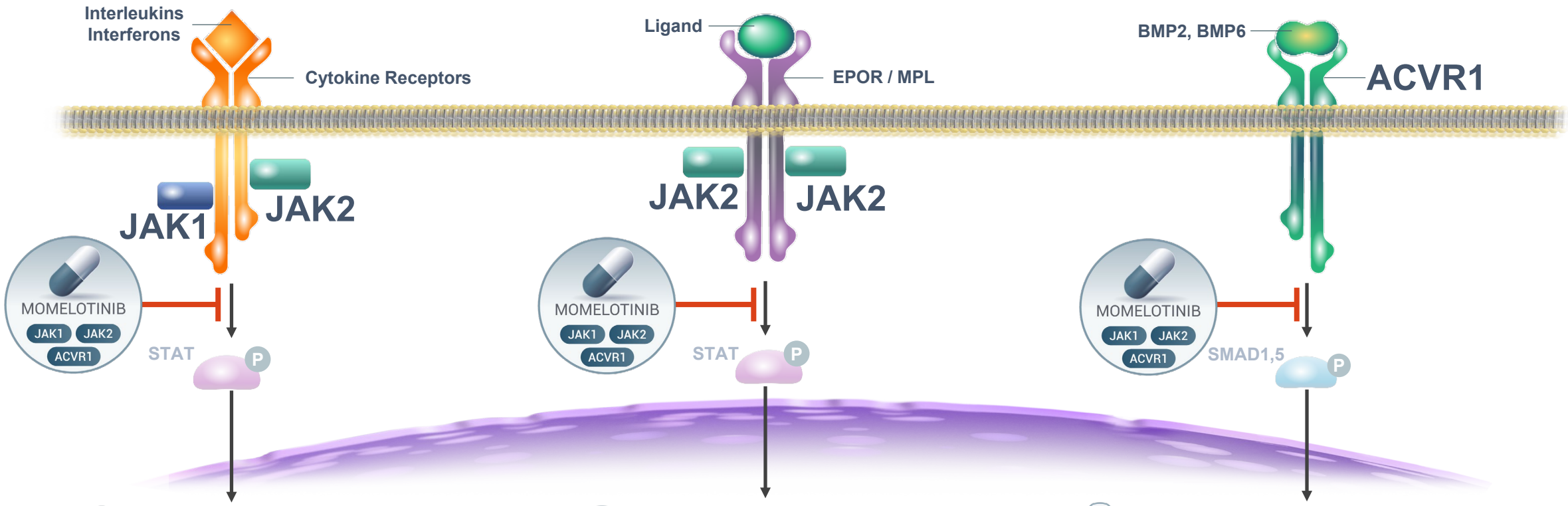


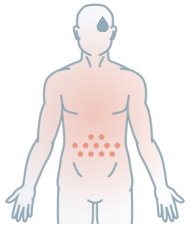
- Clonal proliferation leading to extramedullary hematopoiesis and burdensome **splenomegaly**



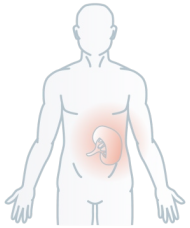
- Aberrant activation of hepcidin transcription via hyperactivated ACVR1 signaling resulting in profound **functional iron deficiency anemia**

Myelofibrosis Biology:
Momelotinib Uniquely Inhibits All Three Disease Drivers

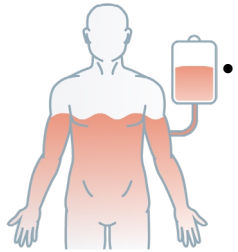




- Decreased inflammation and aberrant cytokine signaling **improves constitutional symptoms**

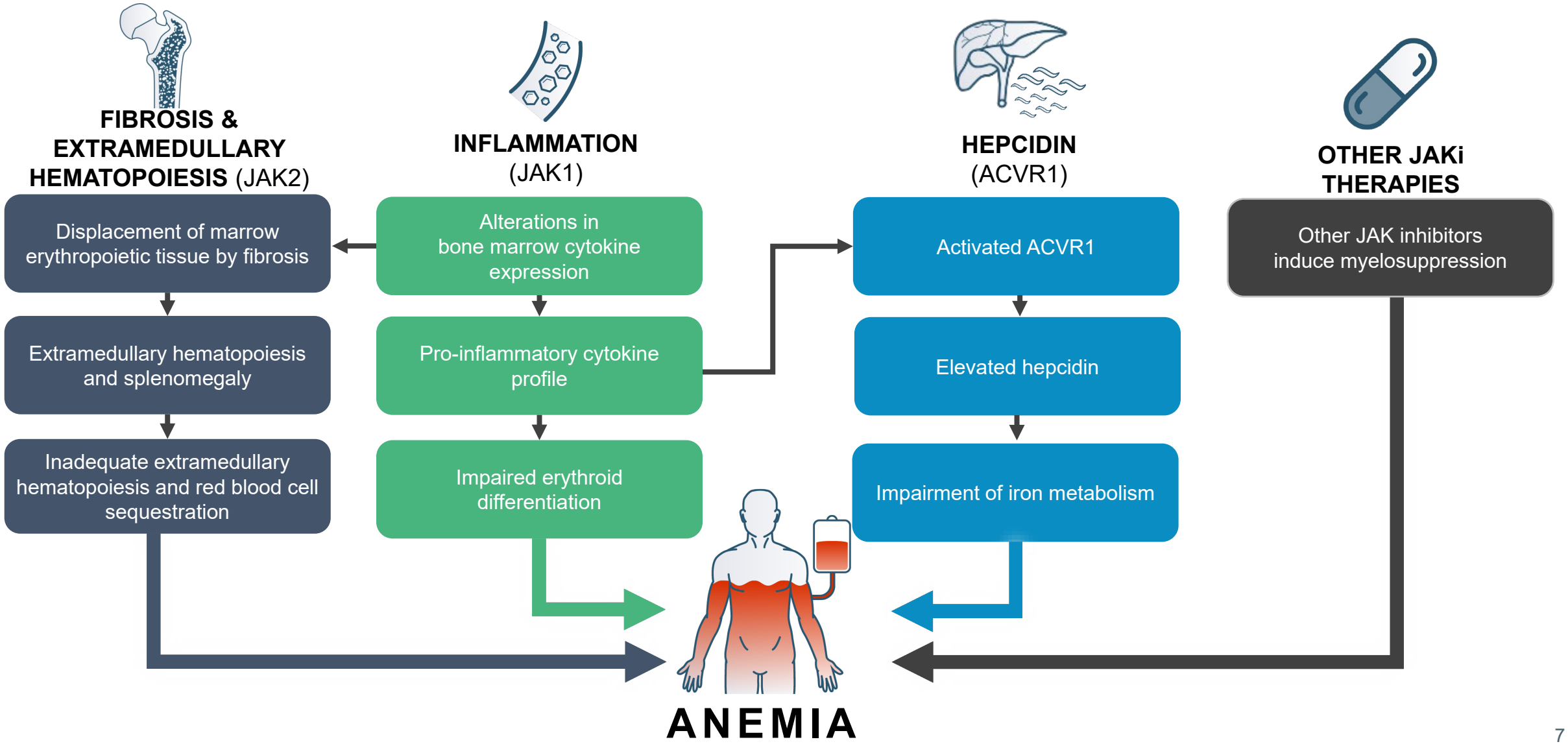


- Reduced extramedullary hematopoiesis **improves splenomegaly**



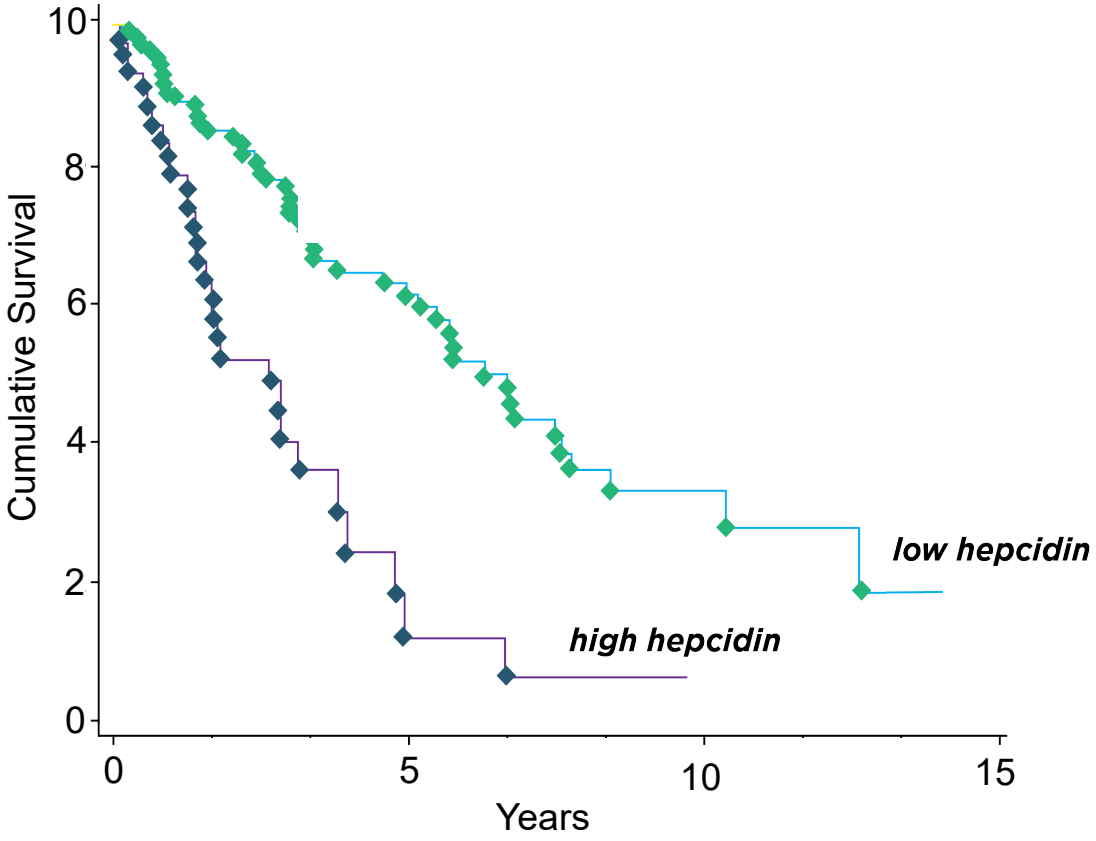
- Decreased hepcidin transcription restores iron homeostasis and **increases hemoglobin** leading to array of anemia benefits

Myelofibrosis Anemia:
Momelotinib Could Positively Impact Multiple Pathways to Anemia



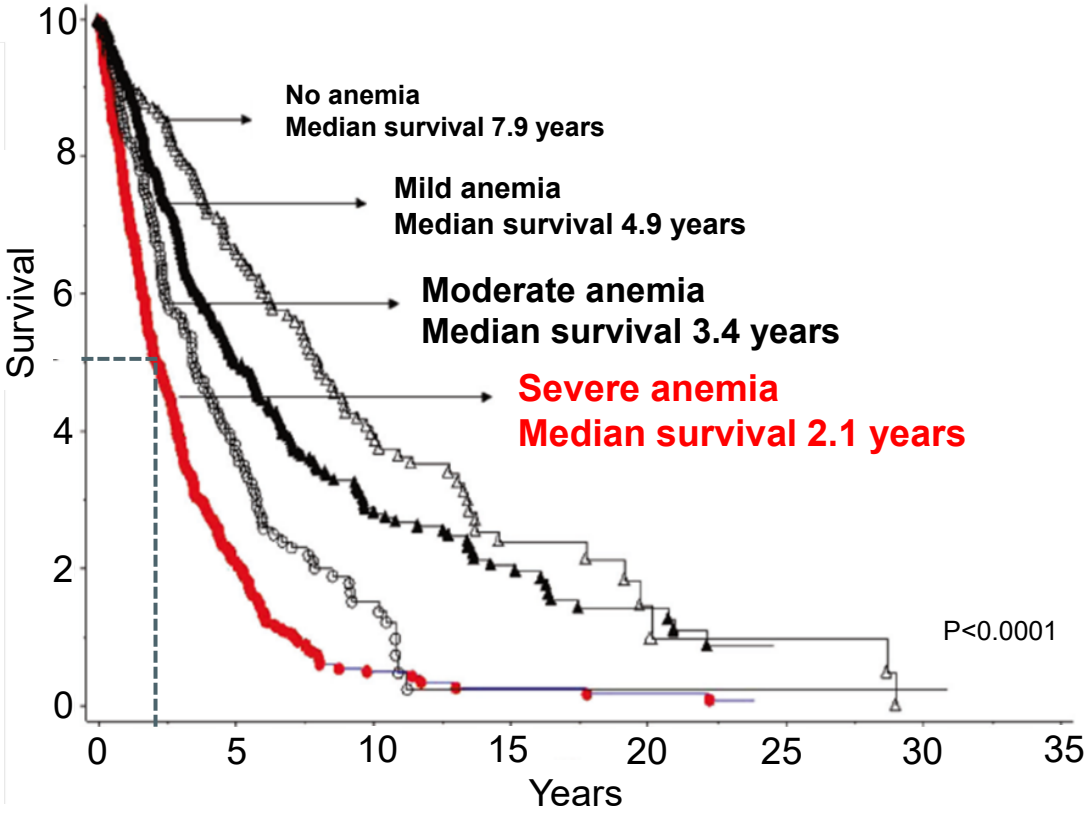
Myelofibrosis Anemia:
High Hepcidin & Severe Anemia Predict Poor Survival

Hepcidin predicts poor survival in myelofibrosis



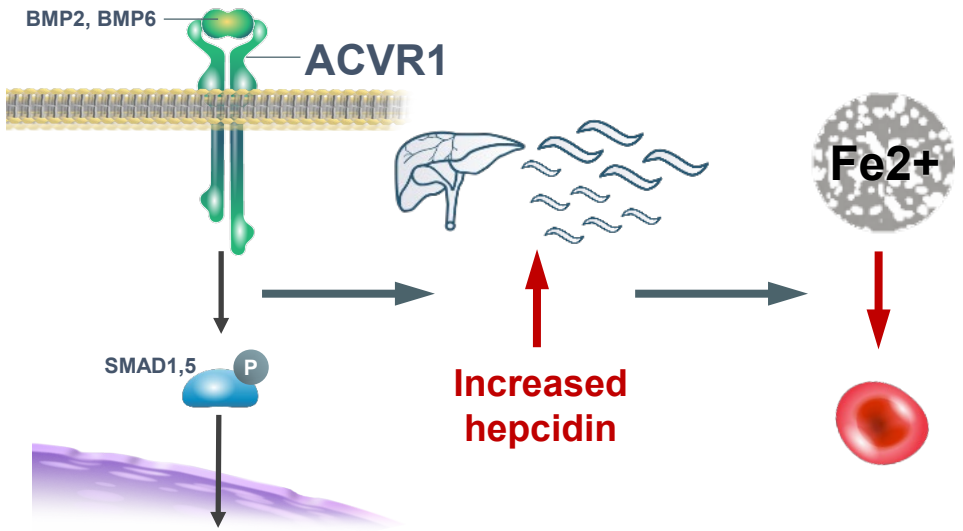
Pardanani et al; *American Journal of Hematology 2013*

Anemia predicts poor survival in myelofibrosis

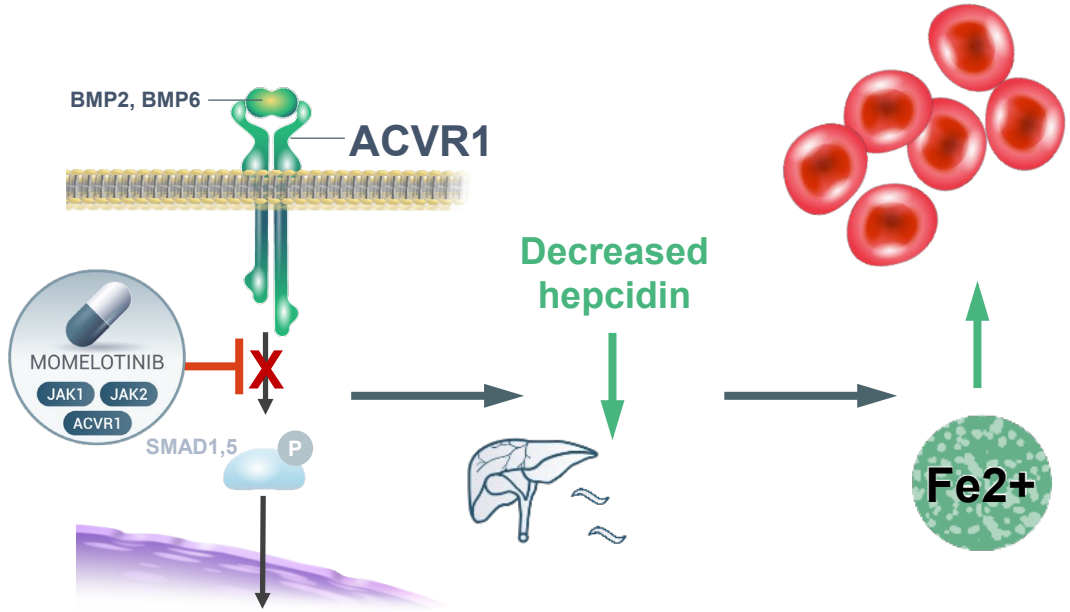


Nicolosi M et al; *Leukemia.* 2018

Myelofibrosis Anemia:
Reducing Hepcidin Restores Red Blood Cell Production



PLASMA IRON **DEFICIENCY**

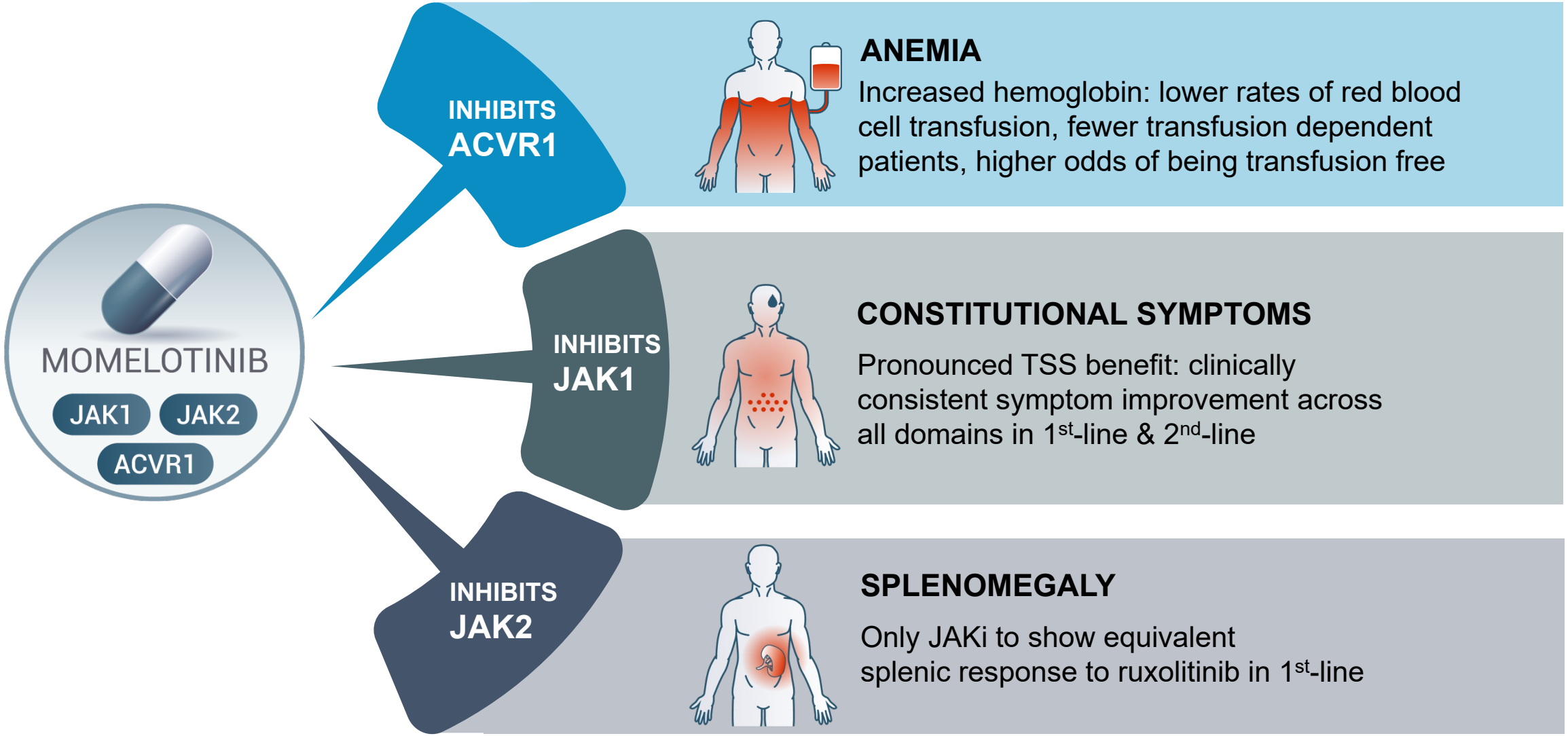


PLASMA IRON **NORMALIZATION**

Momelotinib-mediated plasma iron elevation leads to stimulation of erythropoiesis and red blood cell production

Momelotinib:

SIMPLIFY Data Strongly Support Benefits in Three Hallmarks of Myelofibrosis



MOMENTUM

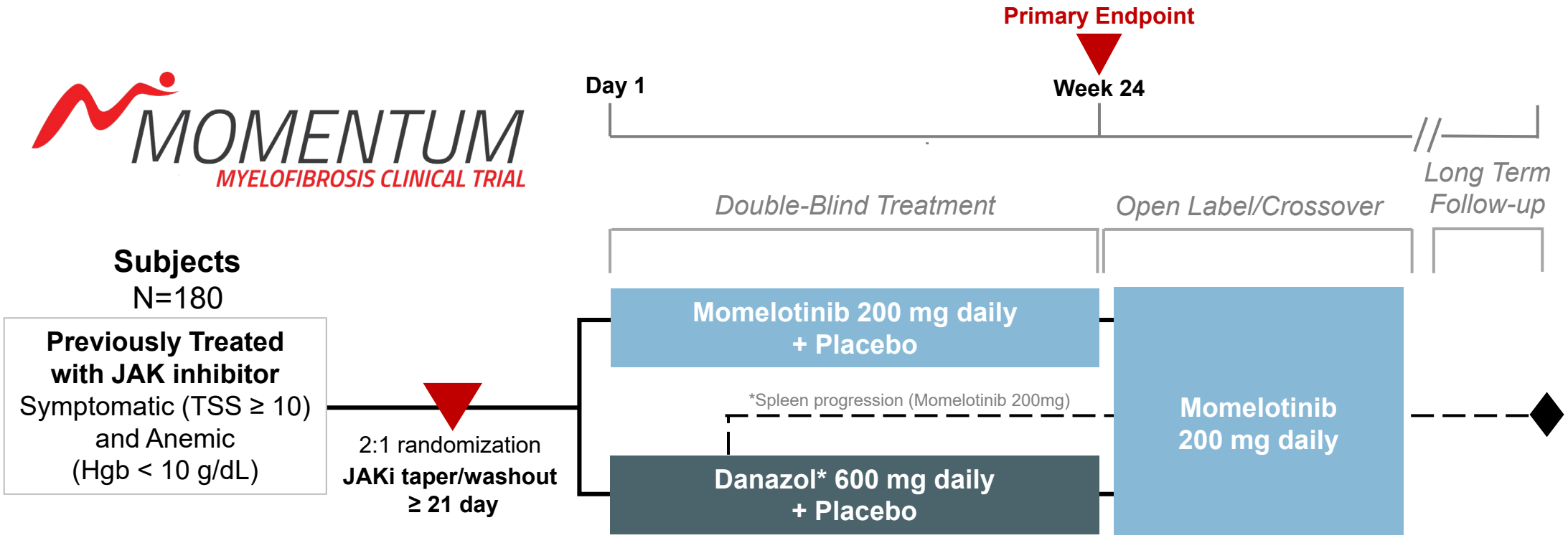
MYELOFIBROSIS CLINICAL TRIAL

Building Momentum for Patients with Myelofibrosis

LAUNCHED Q4 2019!

Momentum P3 Trial:
Phase 3 Registration Trial Schema

A Randomized, Double-Blind, Phase 3 Study to Evaluate the Activity of Momelotinib (MMB) versus Danazol (DAN) in Symptomatic, Anemic Subjects with Primary Myelofibrosis (PMF), Post-Polycythemia Vera (PV) Myelofibrosis, or Post Essential Thrombocythemia (ET) Myelofibrosis who were Previously Treated with JAK Inhibitor Therapy



*Early crossover to open label in the event of confirmed symptomatic splenic progression

Danazol has been selected as an appropriate treatment comparator given its use to ameliorate anemia in myelofibrosis patients, as recommended by NCCN and ESMO guidelines.

Momentum P3 Trial:
Study Objectives

Primary Endpoint:

- Total symptom score (TSS) response rate of momelotinib vs. danazol at Week 24 in symptomatic and anemic patients with PMF, post-PV myelofibrosis, or post-ET myelofibrosis who were previously treated with an approved JAK inhibitor therapy

Secondary & Exploratory Endpoints:

- Transfusion independence (TI) rate at Week 24
- Splenic response rate (SRR) at Week 24
- Duration of TSS response for subjects treated with momelotinib
- Other measures of anemia benefit, including TD-TI rate and measures of cumulative transfusion burden
- Additional Patient Reported Outcomes, including assessments of fatigue and physical function

Momentum P3 Trial: **Key Design Elements**

Chief Investigator:
Dr. Srdan Verstovsek, MD Anderson Cancer Center, Houston, Texas, USA

Endpoint	Order & Powering	Supporting Data/Rationale
Symptom (TSS) response rate	***Primary (W24)*** 99% powered; p<0.05	FDA preferred measure of clinical benefit in myelofibrosis Consistent and meaningful TSS responses in SIMPLIFY-1 and SIMPLIFY-2
Transfusion Independence rate	***Secondary (W24)*** >90% powered; p<0.05	Favorable and statistically significant TI rates in SIMPLIFY-1 and SIMPLIFY-2
Spleen (SRR) response rate	***Secondary (W24)*** >90% powered; p<0.05	Defined washout allows for splenic rebound and SRR benefit Non-inferior SRR benefit head-to-head vs ruxolitinib in SIMPLIFY-1
Durability of TSS response	***Secondary (W48)***	Durability of symptomatic benefit to W48 established in SIMPLIFY-1 and SIMPLIFY-2
Other anemia measures	***Secondary & Exploratory***	Consistent suite of benefits: TD-TI rates, improved hemoglobin, reduced transfusion frequency, etc.

**Stratified for baseline TSS, RBC transfusions & spleen*

Pronounced **Symptom Benefit**

SIMPLIFY-2

Statistically Significant Symptom Response

Momelotinib compared to best available therapy (~90% ruxolitinib) in 2nd-line patients

26.2% Total Symptom Score (TSS) ✓

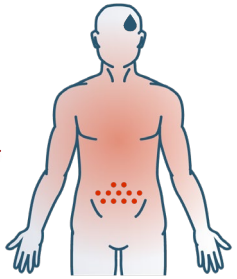
vs 5.9% best available therapy (BAT)

(p < 0.001)

Baseline TSS **was a stratification factor** in SIMPLIFY-2

MOMENTUM MYELOFIBROSIS CLINICAL TRIAL

Primary Endpoint
99% Powered



TSS response is defined as the proportion of subjects who achieve a ≥ 50% reduction in TSS over the 28 days immediately prior to the end of Week 24 compared to baseline

Maintenance of **Transfusion Independence**

SIMPLIFY-1

66% ✓

vs 49% ruxolitinib

Statistically significant
transfusion independence rate
(p < 0.001)

SIMPLIFY-2

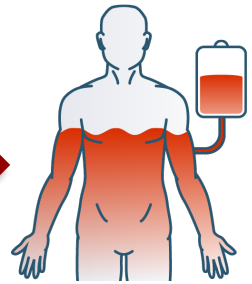
43% ✓

vs 21% BAT
(~90% ruxolitinib)

Statistically significant
transfusion independence rate
(p = 0.001)

MOMENTUM
MYELOFIBROSIS CLINICAL TRIAL

Secondary Endpoint
>90% Powered



Transfusion Independence response defined as the proportion of subjects who were transfusion independent at Week 24, where transfusion independence was defined as the absence of red blood cell (RBC) transfusion and no hemoglobin level below 8 g/dL in the prior 12 weeks

Eliminating Need for Frequent **Transfusions**

Transfusion Dependent Subset Analysis

SIMPLIFY-1

49.1% ✓

vs 28.8% ruxolitinib

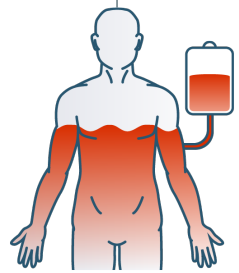
(p = 0.0299)

SIMPLIFY-2

46.6% ✓

vs 18.6% BAT

(p = 0.0048)



≥ 12 Week Transfusion Dependence Response Rate*

Transfusion Dependence response defined as the proportion of transfusion dependent subjects who became transfusion independent for any 12 week or greater period on study, where transfusion independence was defined as the absence of RBC transfusion and no hemoglobin level below 8 g/dL

*Data from Sierra's post-hoc analyses of SIMPLIFY-1 & SIMPLIFY-2 studies

Dramatic Reduction in Odds of Being **Transfused**

*"Overall, these highly persuasive statistical analyses further confirm that **momelotinib treatment elicits a substantive mechanistically-driven anemia benefit.**"*

Dr. Ruben Mesa

Director of the Mays Cancer Center
Home to UT Health San Antonio MD
Anderson Cancer Center

Dec 2019

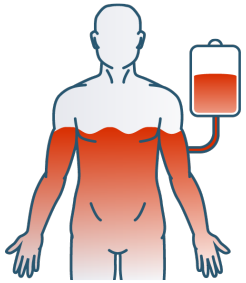
SIMPLIFY-1

Remarkable Reduction in Need for Transfusions

9.3x ✓

Odds of **not being transfused** on momelotinib compared to ruxolitinib

($p < 0.0001$)



ASH 2019
Poster (#1663)

*Data from Sierra's post-hoc analyses of SIMPLIFY-1 & SIMPLIFY-2 studies

Equivalent Clinical Benefit on **Splenomegaly**

SIMPLIFY-1

27%

vs 29% ruxolitinib

(p=0.011)

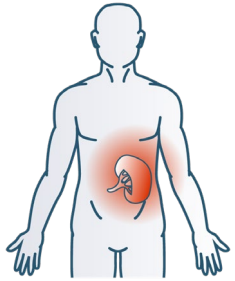
Splenic Response ✓

Momelotinib clinically equivalent to ruxolitinib on spleen

<u>Only</u> JAKi to show comparable spleen response to ruxolitinib

MOMENTUM MYELOFIBROSIS CLINICAL TRIAL

Secondary Endpoint
>90% Powered



Splenic Response Rate (SRR) defined as ≥ 35% reduction in spleen volume at W24 versus baseline

Momelotinib Safety:
Favourable Toxicity Profile

SIMPLIFY-1

Common Adverse Event	Momelotinib	Ruxolitinib
Thrombocytopenia*	19%	29%
Diarrhea	18%	20%
Headache	17%	20%
Dizziness	16%	12%
Nausea	16%	4%
Fatigue	15%	12%
Anemia**	14%	38%
Abdominal Pain	10%	11%

Grade 3 or 4 Adverse Event	Momelotinib	Ruxolitinib
Thrombocytopenia*	7%	5%
Anemia**	6%	23%
Diarrhea	3%	1%
Hypertension	3%	4%
Neutropenia	3%	5%

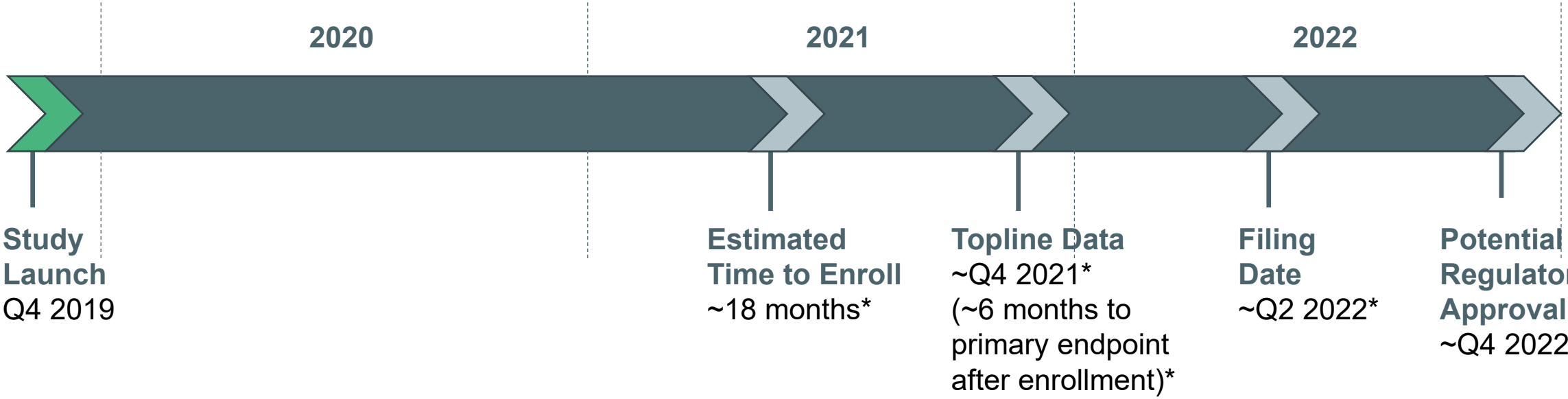
*dose reduction/interruption for thrombocytopenia: Momelotinib = 5.6% Ruxolitinib = 24.5%
**dose reduction/interruption for anemia: Momelotinib = 1.4% Ruxolitinib = 6.0%

	Momelotinib (n=214)	Ruxolitinib (n=216)
AEs	92%	95%
Grade 3 or 4 AE	34%	44%
≥Grade 3 AE Related to Study Drug	21%	29%
Serious AE	23%	18%
Serious AE Related to Study Drug	7%	6%

Momelotinib Safety:

- No Adverse Event concerns flagged in our Regulatory interactions
- No evidence of cumulative toxicity/safety issues in long-term dosing and follow-up

Momentum Phase 3 Trial: **Key Trial Assumptions**



Patients: 180 (2:1 randomization)

Territory: Global study (North America, EU, APAC, etc.)

**Company estimates*

***Assuming priority regulatory review; Fast Track granted June 2019*

Momelotinib:
Totality of Data to Support Potential Registration

MOMENTUM
MYELOFIBROSIS CLINICAL TRIAL

PHASE 3 CLINICAL TRIAL

Pivotal study data
~180 subjects

- Primary endpoint: TSS response rate (99% powered; $p < 0.05$)
- Secondary endpoints:
  - Transfusion Independence rate
  - Spleen (SRR) response rate
  - Durability of TSS response
  - Other anemia measures

SIMPLIFY-1
SIMPLIFY-2

Patient data from completed P3 studies
>550 subjects

- Statistically non-inferior spleen response vs ruxolitinib (S-1; $p = 0.011$)
- Statistically significant TSS response vs BAT/ruxolitinib (S-2; $p < 0.001$)
- Statistically significant transfusion independent rates (S-1; $p < 0.001$) (S-2; $p = 0.001$)
- Crossover data: momelotinib efficacy and safety data in patients who switch from ruxolitinib (S-1) or BAT/ruxolitinib (S-2) after Week 24

XAP
EXTENDED ACCESS PROGRAM

Long term treatment data

- Durable response data (some patients treated >8 years)
- Long term safety and tolerability data

Momelotinib Market Opportunity*

Diagnosis

- ~50K patients living with myelofibrosis
- ~75% are intermediate/high risk

1st-Line

~70% receive 1st-line treatment

- ~25% of Int/High risk myelofibrosis patients are transfusion dependent at diagnosis

2nd-Line

>75% will need 2nd-line treatment

- >70% of Int/High risk myelofibrosis patients have anemia
- >50% of patients are transfusion dependent

Favorable patent exclusivity

- potential extensions to 2040** provide a compelling commercial opportunity

**Company estimates*
***assumes anticipated 5 years PTE and SPC extensions*

Clinician Enthusiasm For Momelotinib Supports 1L & 2L Market Opportunity

*"The dual mechanism and clinical data… point to a strong anemia benefit, so I would definitely look to prescribe this in my **front-line** patients who have severe anemia"*

US High Volume Prescriber*
February 2020

*"Transfusions can be a major problem for patients and this product shows a clear benefit for transfusion independence in all studies, so I would use it in the majority of my **front-line** patients with severe anemia"*

EU KOL*
February 2020

*"The majority of patients in **second-line** would potentially be candidates for momelotinib."*

Dr. Srdan Verstovsek
June 2019

Momelotinib Market Opportunity:

- 1L - patients with severe anemia or transfusion dependency
- 2L – broad utility across all patients; particularly anemic/cytopenic

**Sierra market research conducted by 3rd party*

Momelotinib:
Strong Endorsement from Gilead

Improved agreement and commitment from Gilead meaningfully enhances the potential long-term value of momelotinib for Sierra and its stockholders:

- Gilead has become a stockholder in Sierra (~7%)
- Blended annual royalty rates payable to Gilead substantially reduced
- Net royalties range from very low double digits (sub-$B revenue) to teens (>$B revenue)
- Milestone payment eliminated that would have been due to Gilead upon initiation of MOMENTUM, further extending our financial resources

“Gilead continues to believe in the potential of momelotinib, and we are pleased that Sierra will continue development of the compound in hopes that it will benefit patients in the future."

Andrew Dickinson, Chief Financial Officer of Gilead

Late Stage Drug Development Company Oriented to Potential Registration and Commercialization

- Momelotinib – differentiated JAKi potentially addressing all three hallmarks of myelofibrosis
  - MOMENTUM Phase 3 in 2nd-line myelofibrosis launched in Q4 2019
- Highly experienced management team with proven track record in drug development
- Strong financial standing:
  - $147.5M in cash and cash equivalents (as of December 31, 2019)
  - Key investors include Vivo Capital, Longitude Capital, OrbiMed and Abingworth
  - Topline data warrant: Expires 75 days post-announcement; Potential ~$34M in additional funding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NASDAQ: SRRA