INVESTIGATIONAL PIM1 INHIBITOR NUVISERTIB IN COMBINATION WITH MOMELOTINIB SHOWED PROMISING CLINICAL ACTIVITY IN PATIENTS WITH MYELOFIBROSIS AND ANEMIA: DATA FROM AN ONGOING GLOBAL PHASE 1/2 STUDY

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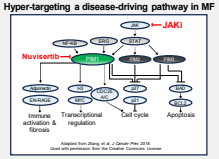
INTRODUCTION

- **PIM1**, downstream of JAK/STAT, is regulated by multiple transcription factors (e.g., NF-kB, ERG, etc.)
- **Dual inhibition of JAK and PIM1** may provide more comprehensive suppression of these combined disease-relevant pathways

Hyper-targeting a disease-driving pathway in MF



- **Momelotinib (MMB)**, a JAK1/JAK2/ACVR1 inhibitor approved for MF patients with anemia, demonstrated a TSS50 of 25%, SVR25 of 39% at Wk24, and anemia improvement in patients with MF previously treated with a JAK inhibitor[1]
- **Nuvisertib (nuvi)**, an oral investigational selective PIM1 inhibitor, under fasted conditions showed promising preliminary single agent clinical activity including best TSS50 of 45% and best SVR25 of 20% in patients with relapsed/refractory MF[2]
  - Higher plasma exposure of nuvi was observed under fed conditions vs. fasted in normal healthy volunteers
- Preliminary data of nuvi (under **fasted** conditions) and MMB combination showed TSS50 of 42% and SVR25 of 50%, and anemia improvement at Wk24[3]
- Here, we present preliminary data of nuvi (under **fed** conditions) and MMB combination for the first time

STUDY DESIGN

Study Population
- Primary, Post-PV, Post-ET MF
- Previously treated with a JAK inhibitor (except momelotinib)

Dose Escalation
Nuvisertib 240–720 mg BID **with food (FED)**
+
Momelotinib 200 mg QD

Dose Expansion

Key Eligibility
- DIPSS Intermediate- 1, 2, or high-risk
- **Platelet count ≥50 x 10^9/L**
- **Hemoglobin <10 g/dL**
- ECOG Performance Status ≤1
- Splenomegaly (≥450 cm^3 by MRI/CT)
- At least 2 symptoms measurable with each score ≥3 or a total score of ≥10 per MF-SAF v4.0

Endpoints
- **Primary:**
  - Safety and tolerability
- **Secondary**
  - Spleen volume reduction (SVR)
  - Total symptoms score (TSS) reduction
  - Overall survival
  - Bone marrow fibrosis change
  - Pharmacokinetics

- Please refer to ClinicalTrials.gov (NCT04176198) for further information

ACKNOWLEDGEMENT

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- Funding source: Sumitomo Pharma America, Inc.
- Momelotinib source: GSK plc.

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1. Verstovsek et al, *Lancet. 2023*
2. Rein et al, *ASH2025, Poster # 2018*
3. Mascarenhas et al, *ASH2025, Oral Presentation #482*
4. Anderson, et al. *Am J Jematol. 2015*

RESULTS

Preliminary data as of 06Dec2025

Baseline Demographics and Disease Characteristics

Patient Characteristics (n=26)	
Age, years, median (range)	71 (56–86)
Male (n, %)	14 (54)
Spleen length, cm, median (range)	9.5 (3–33)
Spleen volume, cm^3, median (range)	1468 (484–5428)
Total Symptoms Score (TSS) (MFSAF v4.0), median (range)	23.4 (11–57)
Platelet Count	
x10^9/L, median (range)	150 (61–488)
≥100 x 10^9/L (n, %)	17 (65)
<100 x 10^9/L (n, %)	9 (35)
Hemoglobin, g/dL, median (range)	8.95 (4.5–10.6)
Transfusion Requiring[a] (n, %)	12 (46)
Disease Characteristics (n=26)	
Myelofibrosis Subtypes (n, %)	
Primary	10 (39)
Post-PV	6 (23)
Post-ET	10 (39)
DIPSS Risk Group (n, %)	
Int-1	2 (8)
Int-2	17 (65)
High	7 (27)
Mutation Type (n, %)	N=17
JAK2 V617F	12 (71)
CALR	4 (24)
MPL variants	3 (18)
HMR[b]	7 (41)
No. of Prior JAK inhibitors (n, %)	
1	21 (81)
≥2	5 (19)
Duration of Prior JAK Inhibitors (n, %)	
<6 months	2 (8)
6–12 months	4 (15)
>12 months	20 (77)

[a]Defined as requiring any units of RBC transfusion over 12 weeks period before C1D1; [b]HMR (high molecular risk) mutations: defined as ASXL1, SRSF2, EZH2, IDH1/2, and U2AF1)

Dose Escalation/Enrichment Cohorts (N=26)

Dose of Nuvisertib (FED) + Momelotinib 200 mg QD	Number of Patients	DLT
240 mg BID	9	None
360 mg BID	6	None
480 mg BID	8	None
720 mg BID	3	None

- No DLTs occurred; MTD not reached, enrollment ongoing

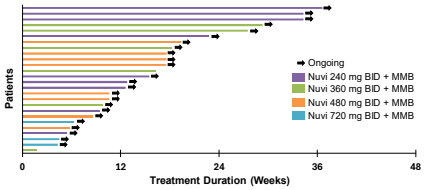
Treatment-emergent Adverse Events (N=26)

AE Preferred Term	Grade 1	Grade 2	Grade 3[a]	Total
Non-hematologic TEAEs (n, %)				
Nausea	10 (38.5)	1 (3.8)	0	11 (42.3%)
Diarrhoea	4 (15.4)	2 (7.7)	0	6 (23.1%)
Constipation	5 (19.2)	1 (3.8)	0	6 (23.1%)
Hematologic TEAEs (n, %)				
Platelet count decreased	0	3 (11.5)	3 (11.5)	6 (23.1%)[b]

[a]No grade 4 or 5 events were reported; [b]3/6 patients had reduced platelets at baseline

- The most common adverse events were Grade 1/2 nausea, diarrhoea and constipation; these were transient and manageable with supportive care
- Nuvi (fed) + MMB appears to be generally well tolerated
- No new safety signal identified

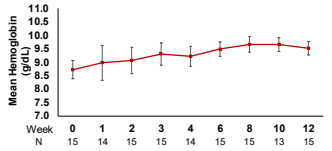
Nuvi + MMB Showed Sustained Clinical Benefit



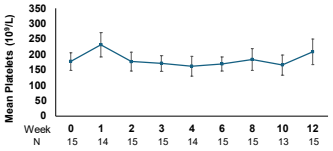
- 24 of 26 patients remain on active treatment
- Reason for treatment discontinuation in 2 pts was "withdrawal by subject"
- Median duration of treatment is 14 weeks (range 2–37)

Hemoglobin Improvement with 53% Anemia Response and Platelet Stability

Hemoglobin Improvement N=15; Mean±SEM



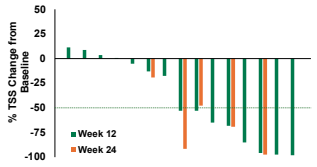
Platelet Stability N=15; Mean±SEM



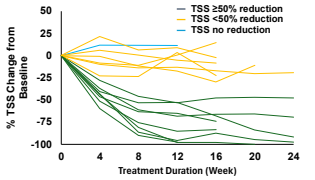
- 8 out of 15 (53%) evaluable patients[a] showed anemia response per IWG ELN2024 at any time: 4 major responses and 4 minor responses

Early and Sustained TSS Responses Observed with Nuvi + MMB

Changes in Total Symptom Score TSS50: 8/15[a] (53%) at Wk12, 3/5[b] (60%) at Wk 24



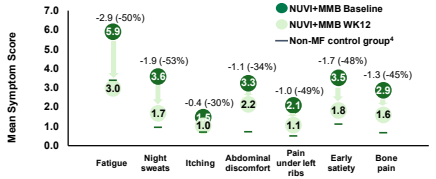
Early and Sustained Symptom Reduction (N=15[a])



- Median % TSS change: –53% (range 11% to –98%); TSS50 at Wk12: 53% (8/15) and at Wk24: 60% (3/5)

Individual Symptom Improvement

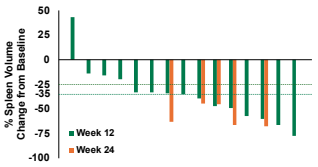
Absolute Changes in Individual Symptoms at Wk12 (N=15[a])



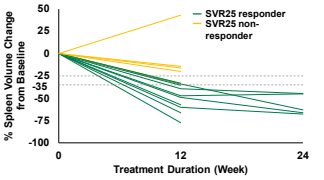
[a]Efficacy evaluable: on ≥Wk12 treatment or discontinued due to treatment related AE or disease progression [b]Patients with Wk24 data

Spleen Responses Observed with Nuvi + MMB

Changes in Spleen Volume SVR25: 11/15[a] (73%) at Wk12, 5/5[b] (100%) at Wk 24



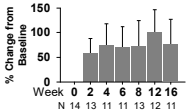
Early and Deep Reduction in Spleen Volume (N=15[a])



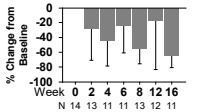
- Median % SVR change: –35% (range 43% to –77%); SVR25 at Wk12: 73% (11/15) and at Wk24: 100% (5/5)

Cytokine Modulation Observed with Nuvi + MMB

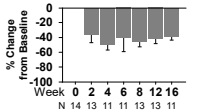
↑ Adiponectin (anti-inflammatory) N=14 (Median, IQR)



↓ EN-RAGE (pro-inflammatory) N=14 (Median, IQR)



↓ IL-8 (pro-inflammatory) N=14 (Median, IQR)



CONCLUSIONS

- Nuvisertib, an oral investigational selective PIM1 inhibitor, showed promising preliminary single agent clinical activity in patients with R/R MF
- Preliminary data from the ongoing Phase 1 dose escalation study of Nuvisertib (under fed conditions) and Momelotinib combination in pts with R/R MF and anemia showed,
  - Combination appears well tolerated without any new safety signals
  - Early and sustained TSS responses and improvement in all individual symptoms
  - Early and sustained spleen responses
  - Hemoglobin improvement with 53% anemia response and platelet stability
  - Cytokine modulation: increased anti-inflammatory (e.g., adiponectin) and decreased pro-inflammatory (e.g., EN-RAGE, IL-18)
- Preliminary data support ongoing clinical development of nuvisertib (under fed conditions) in combination with momelotinib in MF