Phase 1/2 Study of NS-018, an Oral JAK2 Inhibitor, in Patients with Primary Myelofibrosis (PMF), Post-polycthemia Vera Myelofibrosis (post-PMF V), and Post-essential Thrombocythemia Myelofibrosis (post-ET MF)  
Srdan Verstovsek, MD, PhD,1 Moshe Talpaz, MD,2 Ellen Ritchie, MD,3 Martha Wadleigh, MD,4 Olatoyosi M. Odenike, MD,5 Catrina Jamieson, MD, PhD,6 Brady Stein, MD,7 Candido E. Rivera, MD,8 Tomonori Uno, PhD,9 Ruben A. Mesa, MD10  
1Department of Leukemia, University of Texas MD Anderson Cancer Center, Houston, TX; 2Cancer and Leukemia Group B, Ann Arbor, MI; 3Cornell University, New York, NY; 4Dana-Farber Cancer Institute, Boston, MA; 5University of Chicago Medical Center, Chicago, IL; 6Moses Cancer Center, University of California, San Diego, CA; 7Northwestern University Feinberg School of Medicine, Chicago, IL; 8Mayo Clinic, Scottsdale, AZ

INTRODUCTION  
Myelofibrosis (MF) is a rare clonal myelo- and megakaryocytic disorder that leads to fibrosis of the marrow, splenomegaly, anemia, and increased thrombocytosis.1 MF has traditionally been classified into primary MF (PMF) and secondary MF (post-PMF) based on the presence or absence of prior polycythemia vera (PV).2 In PMF, the underlying cause is chronic myeloproliferative neoplasm (PMN) with the BCR-ABL1 fusion gene.3 Primary post-PMFMF is associated with a genetic translocation involving JAK2 (JAK2V617F).4

METHODS  
Here, we report the safety and efficacy data of the dose-expansion Phase 2 portion of the study. A total of 29 patients were treated with NS-018 300 mg QD in the Phase 2 portion. Treatment response was assessed according to the International Working Group—Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) criteria.5

RESULTS  
The majority of patients were IPSS high risk (52%) and 13 (45%) patients had baseline cytopenias.6–8

Efficacy  
Clinical response: Symptoms  
Among 26 patients evaluable for response assessed by ELN/ITF, 7 (27%) achieved ≥10% reduction in spleen volume (Figure 3).  
— 8 patients maintained response for ≥6 months.  
— Patients achieving ≥10% reduction in spleen volume were by ELN/ITF were assessed as achieving ≥10% reduction in spleen volume by ELN/ITF.  
— Two patients attained ≥50% reduction in spleen volume with improved quality of life and survival,12,13 was achieved with improved quality of life and survival.

Safety  
Adverse events (AEs) were graded according to National Cancer Institute Common Toxicity Criteria (version 4.0).4

Clinical response: blood counts  
Among 3 patients who were transfusion dependent at baseline, one became transfusion independent by 12 weeks, and two of these cases of anemia considered possibly related to NS-018 treatment.

Pharmacodynamics  
Fold change in mean fluorescence intensity of CD38/CD19+ PBMCs. CD38 is a known JAK2 substrate. 

DISCUSSIONS  
In this Phase 2 study, NS-018 300 mg QD was generally well tolerated. 
— Anemia or thrombocytopenia did not worsen by >1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

REFERENCES  

ACKNOWLEDGMENTS  
The study is funded by NS Pharma, Inc., a subsidiary of Hiroyuki Shipyo Co., Ltd. The authors received editorial support from Adelphi Communications Ltd, funded by NS Pharma, Inc. The study is sponsored by BMS-Thrombotic Therapeutics in the development of its strategy for the development of the clinical and pathophysiology.

CONCLUSIONS  
— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Two patients attained ≥50% reduction in spleen volume with improved quality of life and survival.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.

— Anemia or thrombocytopenia did not worsen by ≥1 grade from baseline; hemoglobin levels were generally stable with NS-018 treatment.

— In the Phase 2 study, NS-018 300 mg QD was generally well tolerated.