

# RIGOSERTIB - Lead Candidate for Onconova Therapeutics

## Phase 3 stage molecule targeting RAS Pathways:

Rigosertib, a Phase 3 stage small molecule, blocks cellular signaling by blocking Ras effector pathways. The initial focus for Rigosertib is Myelodysplastic Syndromes (MDS), a group of bone marrow disorders that converts to acute myeloid leukemia in approximately 30% of patients. Phase 3 trials for IV Rigosertib are being conducted on four continents: the US, Europe, Asia, and Australia. Onconova is also developing an oral form of Rigosertib in combination with azacitidine as first line therapy for all MDS patients. The Company recently completed a successful end of Phase 2 meeting with the FDA for this combination therapy and a Phase 3 trial design is expected in the near term. Both IV and oral rigosertib are protected by issued patents worldwide and have been granted orphan drug designation in the US, Europe and Japan for MDS.

### PARTNERSHIPS

- Partnership with SymBio (Tokyo, Japan) to develop and commercialize Rigosertib in Japan and Korea
- Additional partnership discussions underway

### CLINICAL DEVELOPMENT

#### Lead Program - IV Rigosertib in Higher Risk MDS Patients

A Phase 3 international, randomized controlled study of Rigosertib versus physician's choice or treatment in patients with myelodysplastic syndromes after failure of a hypomethylating agent. The primary objective of this study is to compare the overall survival (OS) of patients receiving intravenous (IV) Rigosertib to the OS of patients receiving the physician's choice of treatment (PC) in a population of patients with MDS after failure of treatment with a hypomethylating agent, azacitidine (AZA) or decitabine (DEC).

#### Second Program in 1<sup>st</sup> line MDS- Combination Oral Rigosertib + Azacitidine

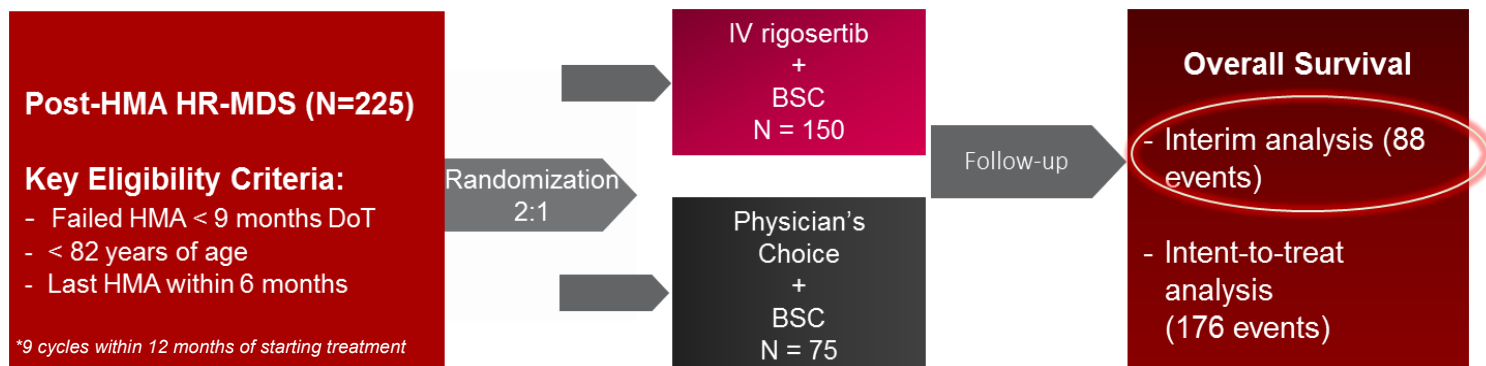
Following evaluation of 54 enrolled patients in the Phase 2 Trial 09-08 of oral Rigosertib plus azacitidine, Onconova conducted an End-of-Phase 2 meeting during which updated results from this trial were discussed with the FDA. Based on these discussions, and guidance from the Agency, Onconova will design a randomized, controlled Phase 3 clinical trial comparing the combination of oral Rigosertib plus azacitidine to azacitidine plus placebo in hypomethylating agent (HMA) naïve HR-MDS patients.

#### IV Formulation (Phase 3 INSPIRE enrolling)

- Continuous infusion using a portable pump
- >500 patients treated in trials
- Lead indication 2nd-line HR-MDS

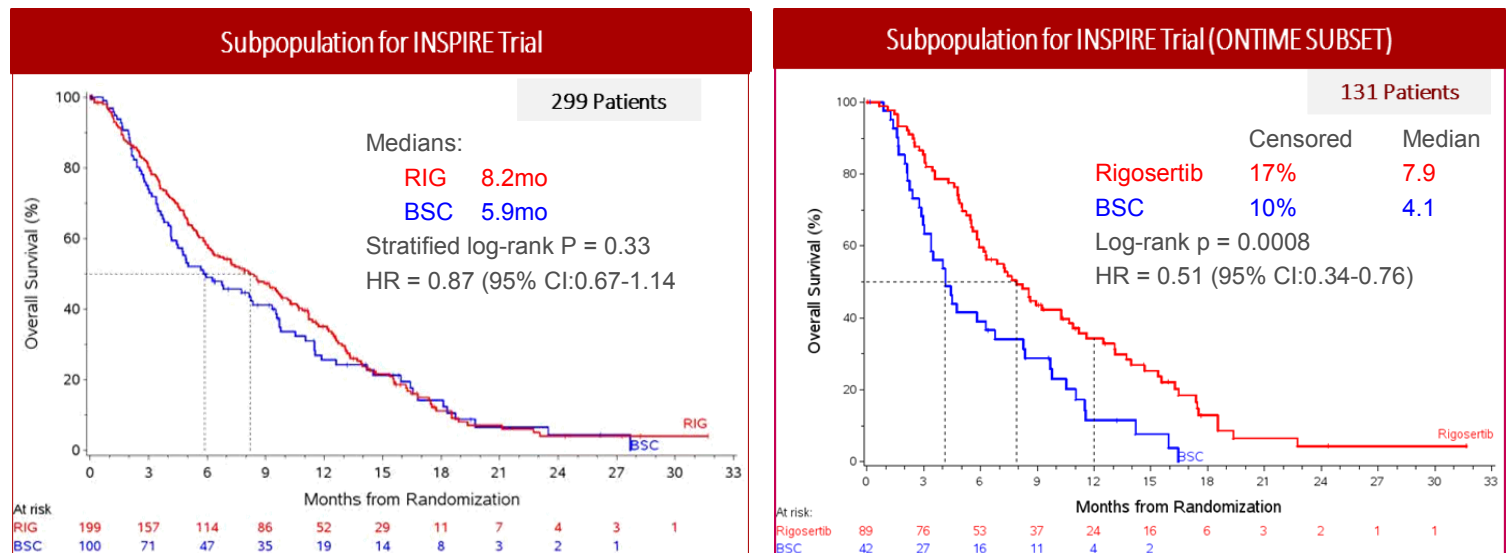


### INSPIRE GLOBAL PHASE 3 STUDY SCHEMA



# PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

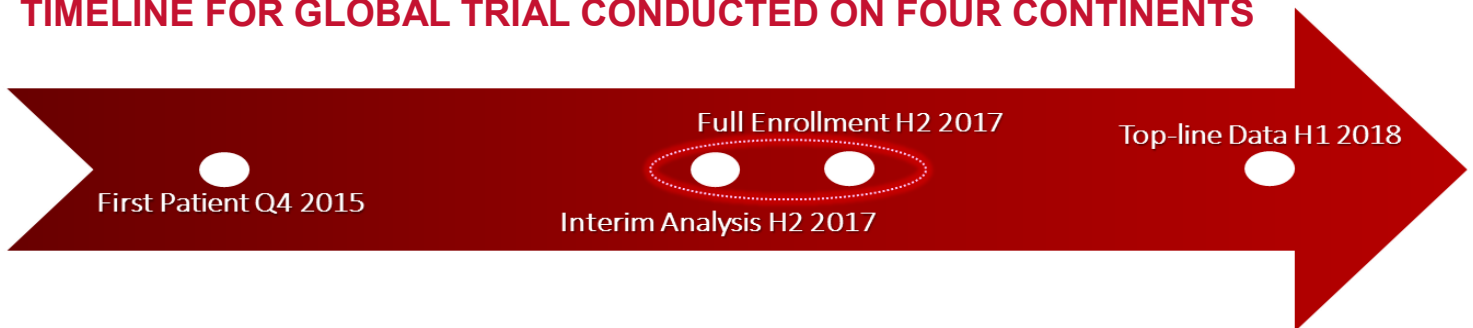

Data from ONTIME paper\* published in Lancet Oncology



ITT OS analysis of ONTIME – HR= 0.87; NS survival benefit; ITT OS of proposed INSPIRE population – HR = 0.48; P = 0.0008

\*Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, et al. Rigosertib versus best supportive care for patients with higher-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, Phase 3 trial; *The Lancet Oncology* 2016 (17): 496–508

## TIMELINE FOR GLOBAL TRIAL CONDUCTED ON FOUR CONTINENTS

**Oral Combination:**

- Synergy patent issued
- More than 250 patients treated
- Single agent and combination trials
- Phase 2 Combination trial enrolled
- Combination with azacitidine advancing to pivotal trial in 2017

- **Interim Phase 2 data presented at ASH 2016**  
Overall response rate of 85% in 20 patients who did not receive prior HMA  
Complete remission (CR) rate of 35% in the front-line patients  
Overall response rate of 62% in patients who received prior HMA
- **End of Phase 2 meeting with FDA in September 2016**  
FDA input helping design Phase 3 trial for approval of combination product for front-line MDS

**Contact Information**

**CORPORATE**  
Onconova Therapeutics, Inc. Tel: +1 212-897-9666 Email: [info@onconova.us](mailto:info@onconova.us)

**INVESTORS AND MEDIA:**  
Lisa Sher - MBS Value Partners Tel: +1 212-750-5800 Email: [ir@onconova.us](mailto:ir@onconova.us)



Or visit <http://www.onconova.com/>