Onconova Therapeutics, Inc.

Corporate Update

January, 2017

Nasdaq: ONTX

Forward Looking Statements

This presentation contains forward-looking statements about Onconova Therapeutics, Inc. based on management's current expectations which are subject to known and unknown uncertainties and risks. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "should," "approximately" or other words that convey uncertainty of future events or outcomes. Our actual results could differ materially from those discussed due to a number of factors, including, but not limited to, our ability to raise additional financing on favorable terms, the success of our clinical trials and our ability to obtain regulatory approvals and other risk factors outlined in our annual and quarterly reports filed with the Securities and Exchange Commission. We are providing this information as of the date of this presentation and do not undertake any obligation to update any forward-looking statements, whether written or oral, that may be made from time to time, as a result of new information, future events or otherwise except as required by law.

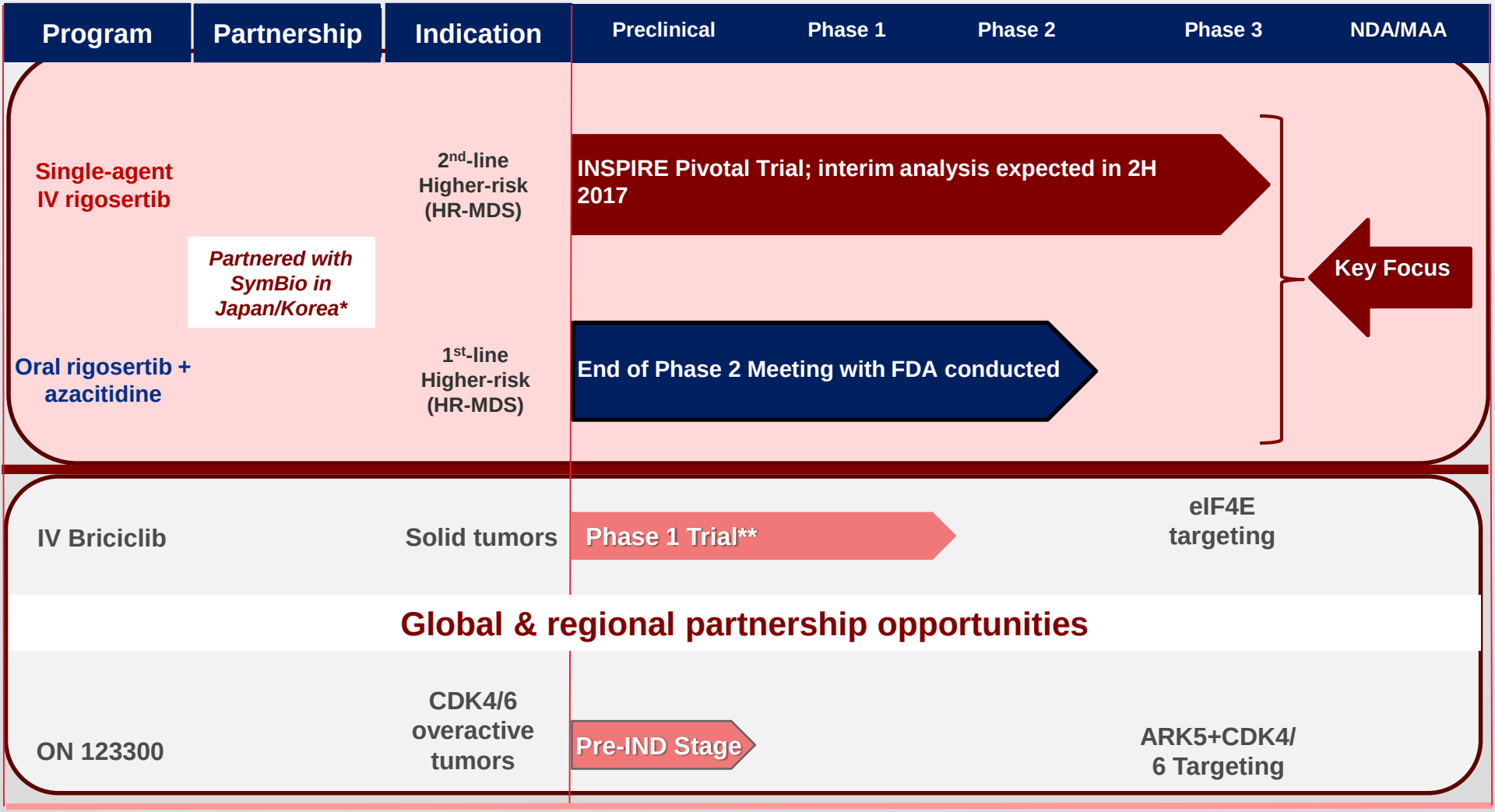
Investment Highlights

- **Addressing an underserved and growing market in MDS**
  - >10,000 patients diagnosed annually
  - No new approved therapies in over 10 years
- **Lead Program: Rigosertib**
  - RAS mimetic - attractive target for MDS and beyond
  - 1,100 patients treated to date
  - Two formulations (Oral and IV)
- **Funded to deliver key 2017 milestones**
  - Oral Phase 2 to enter pivotal trial in 2017
  - IV Phase 3 interim analysis 2H2017; full-enrollment 2H2017; top-line data 1H2018
- **Preclinical pipeline; additional business development opportunities**

Financial Details

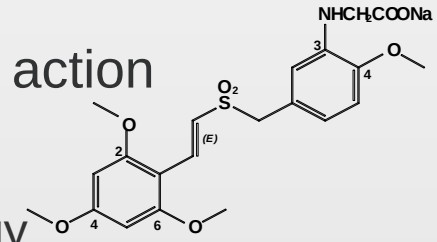
Onconova founded in 1998; public since 2013	
Ticker	Nasdaq, ONTX
Stock information	▪ 6.76 million shares* ▪ Public float 79% ▪ 52 week range $2.11-11.60 ▪ Average daily volume 83,000
Ownership	Tyndall, Tavistock, Sabby, Shire; insiders including management
Analyst coverage	• Maxim (Kolbert/McCarthy); LifeScience Capital (Isaacson) • VLR (Wijma); SeeThru Equity (Tandon)
Debt	0
Liquidity	▪ $ 17.4 million gross proceeds from rights offering in July 2016 ▪ Cash and cash equivalent of $25.8 million* ▪ Sufficient funds for operations thru 2017
Partnerships	• Rigosertib partnered with SymBio Pharmaceuticals in Japan/Korea • Onconova retains US and ROW rights
**As per Q3 financials*	

Onconova Cancer Product Pipeline



Onconova retains rights elsewhere, including USA
***Trial on hold pending partnering and manufacturing of new product lot*

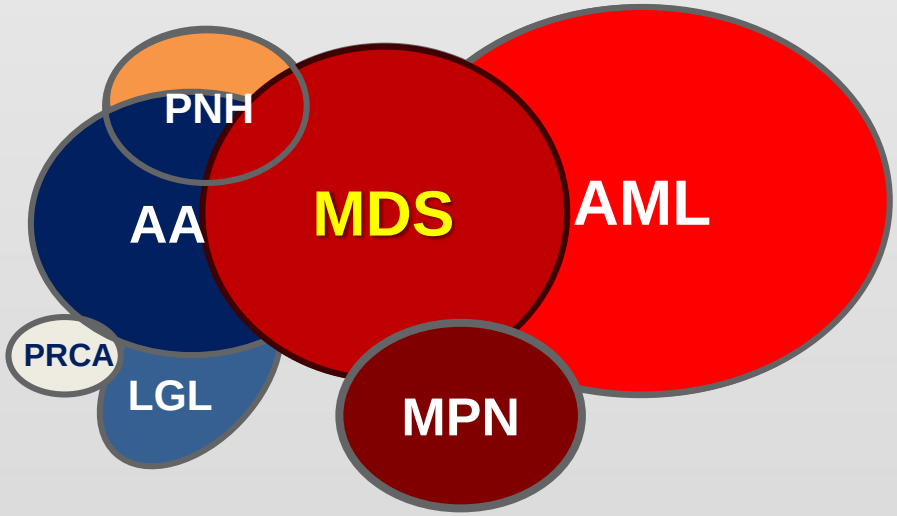
Rigosertib Overview



- Rigosertib is a small molecule with a novel mechanism of action
  - Inhibits cellular signaling by acting as a RAS mimetic
  - RAS gene is one of the most sought after targets in oncology
- Phase 3 INSPIRE trial (IV) enrolling higher-risk MDS patients
  - INSPIRE patient population reflects knowledge from ONTIME Phase 3 trial
  - Pre-planned interim analysis in H2-2017. Top-line data expected in 2018
- Pivotal phase 3 trial protocol in 2017 for rigosertib (oral) + azacitidine
  - Successful End-of-Phase 2 meeting with FDA conducted in September 2016
- Rigosertib has extensive clinical trial database
  - Safety data from more than 1,100 patients (IV & oral)
- Patent protected through 2026 (compound), and 2028 (combination)
  - Orphan drug designation granted in U.S., EU and Japan
  - Partnered in Japan/Korea with SymBio Pharmaceuticals

MDS Overlaps with Other Diseases

- **MDS, a malignant hematopoietic stem cell disorder is characterized by:[1]**
  - Bone marrow failure
  - Cytopenias
  - Tendency to progress to AML



- MDS has overlap with other hematological disorders
- A spectrum of risk, from low to very high, measured by IPSS-R scores.
- US prevalence estimate is 59,000; 18,000 have higher risk MDS
- Treatment options limited to hypomethylating agents (HMAs)
  - Vidaza (Celgene); Dacogen (Eisai/J&J)
  - Both approved a decade ago
- No second-line treatment approved

[1]Young NS. Ann Intern Med. 2002;136:534-546.

Slide credit: clinicaloptions.com

Revised IPSS: Prognostic Score Values and Risk Categories/Scores

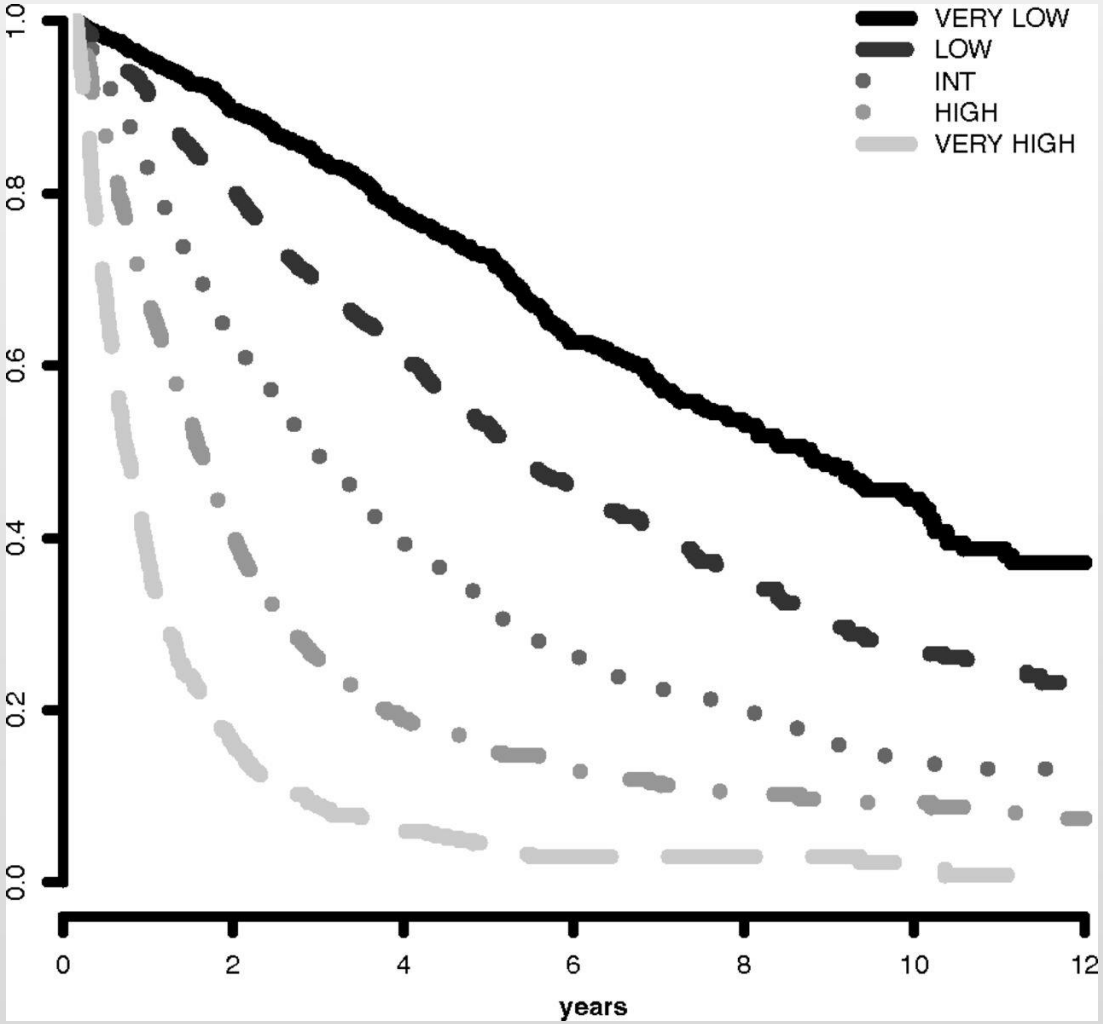
Prognostic Variable	Prognostic Score Value						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good	--	Good	--	Intermediate	Poor	Very poor
BM blast, %	≤ 2	--	> 2 to < 5	--	5-10	> 10	--
Hemoglobin, g/dL	≥ 10	--	8 to < 10	< 8	--	--	--
Platelets, x 10^9/L	≥ 100	50 to < 100	< 50	--	--	--	--
ANC, x 10^9/L	≥ 0.8	< 0.8	--	--	--	--	--

Risk	Score
Very low	≤ 1.5
Low	> 1.5 to 3.0
Intermediate	> 3.0 to 4.5
High	> 4.5 to 6.0
Very high	**> 6**

Greenberg PL, et al. Blood. 2012;120:2454-2465.

Slide credit: clinicaloptions.com

Revised IPSS

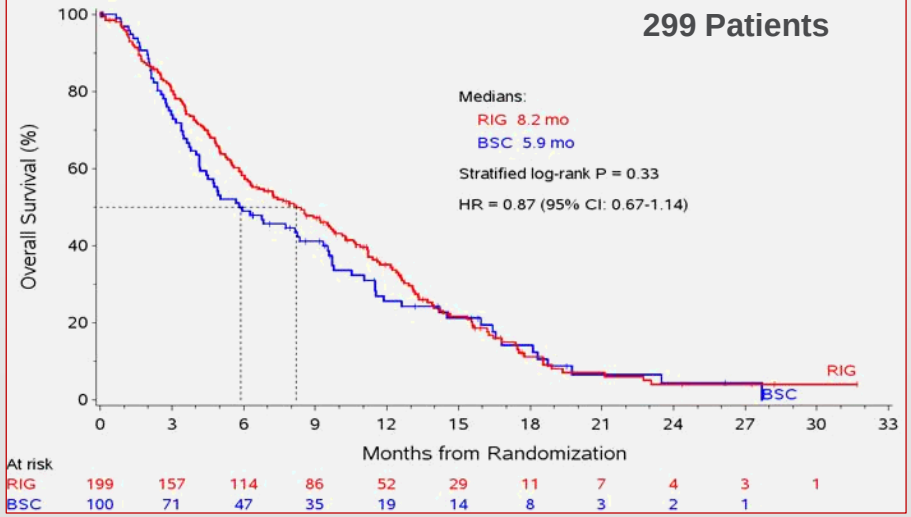


Greenberg et al. Blood 2012;120:2454-65

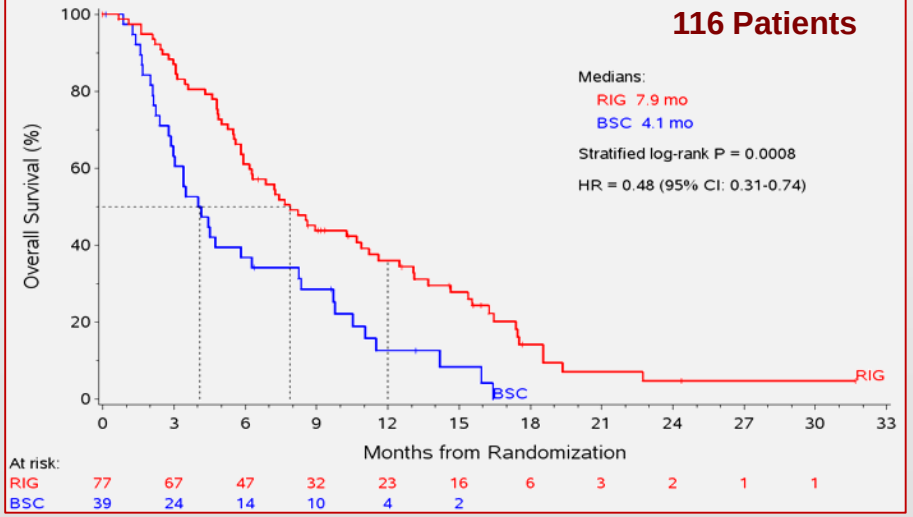
Patient Population for Phase 3 INSPIRE Trial

Data from ONTIME paper* published in *Lancet Oncology*

ITT for ONTIME Trial



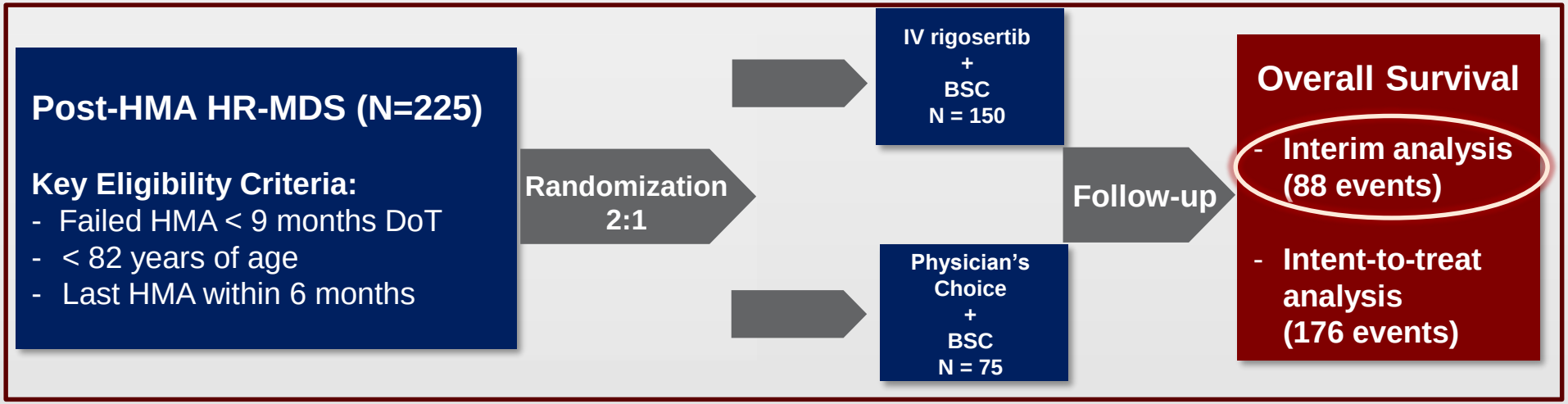
Subpopulation for INSPIRE Trial (ONTIME subset)



- 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

INSPIRE: Global Phase 3 Trial



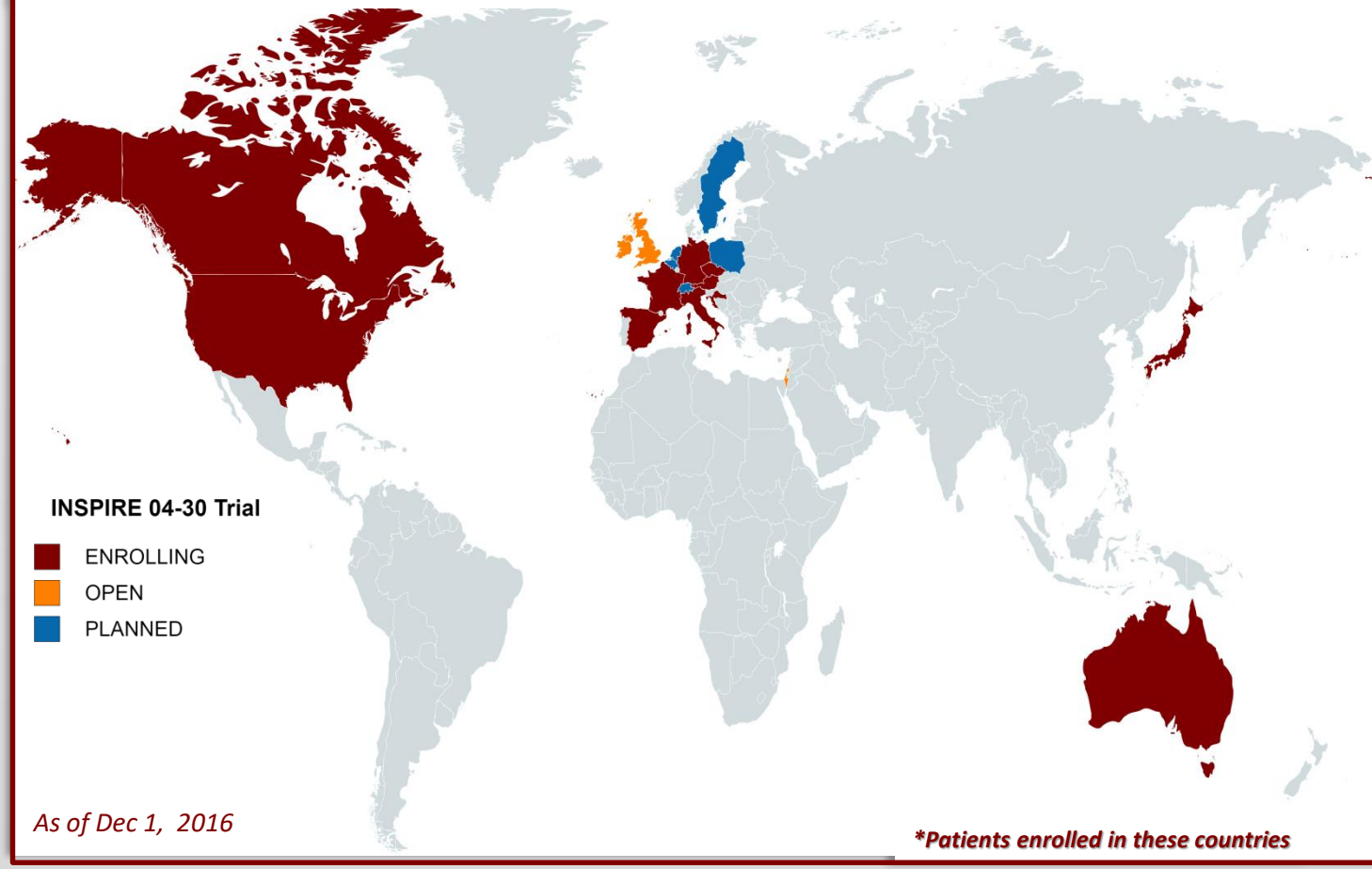
- Statistical analysis: two analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Trial can succeed in two ways: ITT population or IPSS-R Very High Risk
- Genomic sequencing of patient samples

Commentary on new trial in recent publication: Emilio P Alessandrino, Matteo G Della Porta. Novel trial designs for high-risk myelodysplastic syndromes; The Lancet Oncology 2016 (17): 410–412

Global INSPIRE Trial Progress

225 patients; 167 selected sites in 19 countries on 4 continents

*The **IN**ternational **S**tudy of **P**hase III **I**V **R**igos**E**rtib, or INSPIRE, is based on guidance received from the U.S. Food and Drug Administration and European Medicines Agency and derives from findings of the ONTIME Phase 3 trial. Our partner SymBio is enrolling in Japan after discussions with the PMDA.*



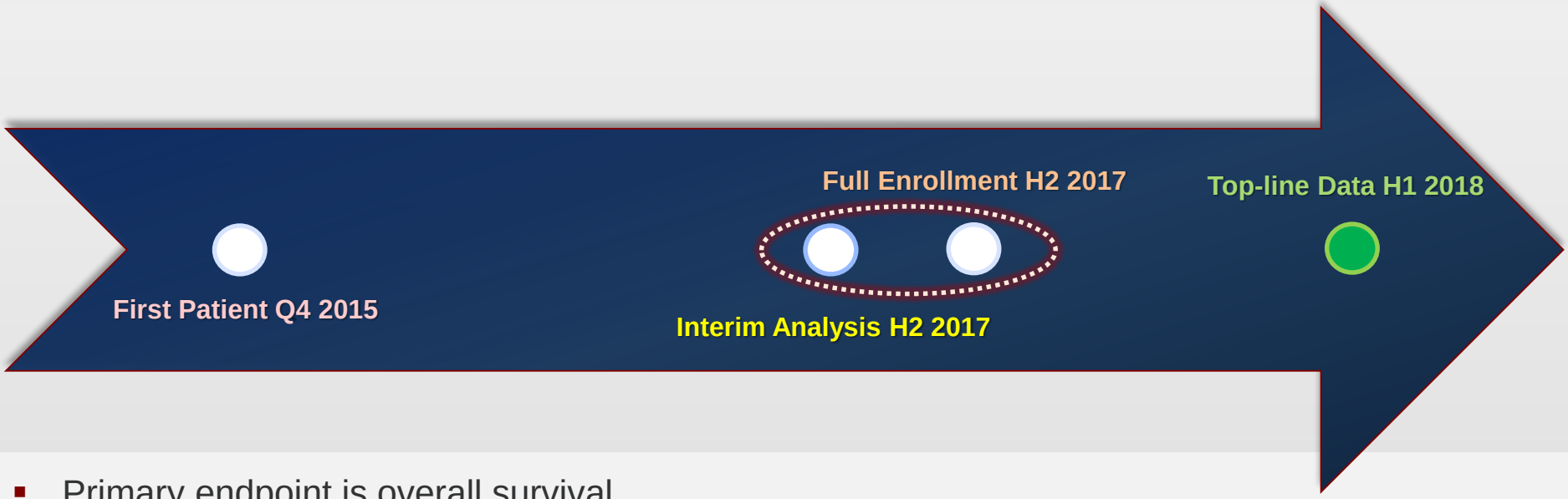
Country	Sites
1. USA*	37
2. Japan*	31
3. Spain*	12
4. Israel	10
5. France*	9
6. Germany*	8
7. Italy*	9
8. U.K.	5
9. Australia*	5
10. Canada*	6
11. Poland*	6
12. Belgium	5
13. Czech Rep.*	5
14. Ireland	4
15. Sweden	4
16. Croatia*	4
17. Austria*	3
18. Netherlands	2
19. Switzerland	2

As of Dec 1, 2016

***Patients enrolled in these countries**

Data Analysis for INSPIRE Trial

Timeline for Global Trial Conducted on Four Continents

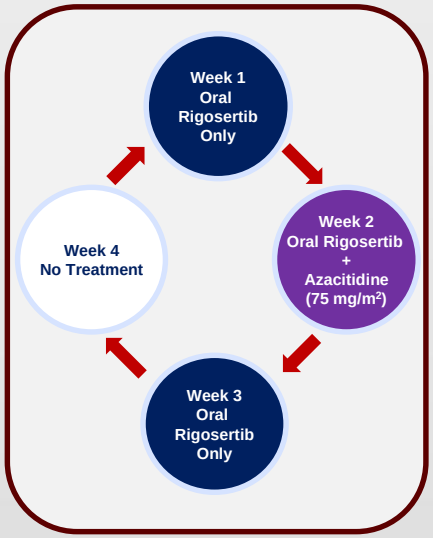


- Primary endpoint is overall survival
  - Entire trial (ITT analysis) after 176 events have occurred
  - If the ITT analysis is negative, a second analysis of IPSS-R VHR subgroup is permitted
- Interim analysis planned
  - ITT analysis after 88 events
  - Types of analysis in discussion as a part of Statistical Analysis Plan
- Secondary analysis includes
  - By region of enrollment (U.S., EU, ROW)
  - Karyotypes; genomics

Updated 09-08 Phase 2 Trial Results

Combination oral Rigosertib + Azacitidine in MDS patients

- Included a diverse patient population including
  - HMA-naïve front-line patients
  - HMA pre-treated second-line patients
  - AML patients
- Phase 2 dose: 560 mg qAM, 280 mg qPM
  - Oral rigosertib twice daily on Day 1-21 (28-day cycle
  - Azacitidine 75 mg/m^2/day SC/IV for 7 days starting on Day 8
- Analysis:
  - CBC was performed weekly
  - Bone marrow aspirate and/or biopsy obtained
    - Baseline, on Day 29, and every 8 weeks thereafter



Phase 2 Efficacy Results for Combination Therapy

Response Criteria	Response per IWG 2006		
	Overall evaluable (N=33)	No prior HMA (N=20)	HMA resistant (N=13)
Complete Remission*	**8 (24%)**	**7 (35%)****	**1 (8%)**
Marrow CR + Hematologic Improvement (HI)	10 (30%)	6 (30%)	4 (31%)
Marrow CR alone	6 (18%)	3 (15%)	3 (23%)
Hematologic Improvement alone	1 (3%)	1 (5%)	0
Stable Disease	8 (24%)	3 (15%)	5 (38%)
Overall IWG Response	**25 (76%)**	**17 (85%)****	**8 (62%)**
Clinical Benefit Response	19 (58%)	14 (70%)	5 (38%)

**All responders had CR and no PR was noted in this study*
***Several published studies show 6-20% CR with single agent azacitidine and overall response of 40-45%*

Phase 2 Rigosertib + Azacitidine

Interim Phase 2 data and End of Phase 2 FDA Meeting

- Overall response rate of 85% in 20 patients who did not receive prior HMA*
  - Complete Remission (CR) rate of 35%
- Overall response rate of 62% in 13 patients who received prior HMA

Key Parameters and Milestones for Oral Rigosertib + Azacitidine Pivotal Program		
Phase 3 Design	Randomized Controlled	1:1 randomization between Aza + placebo and Aza + oral rigosertib
Patient Population	Front-line MDS	Higher risk patients indicated for azacitidine (Vidaza)
Primary Endpoint	**Composite Response**	**Complete and Partial Remission per IWG 2006 criteria for MDS**
Protocol Details	2017	After regulatory discussions are completed

*Navada S, et al. A phase 2 study of the combination of oral rigosertib and azacitidine in patients with myelodysplastic syndrome (MDS). *ASH* 2015; Abstract 910

Recent Achievements and Key Milestones Ahead

2015		1st patient enrolled in U.S. for global Phase 3 INSPIRE trial (IV) of rigosertib for MDS	☑
2016	Mar	Publication of ONTIME (first Phase 3 trial of rigosertib in MDS) results in *Lancet Oncology*	☑
		1st patient enrolled in Europe for INSPIRE trial	☑
	Apr	Publication of rigosertib mechanism of action in *Cell*	☑
	Jul	1st patient enrolled in Japan for INSPIRE trial	☑
		Oversubscribed rights offering closed; gross proceeds of $17.4 million	☑
	Sep	Successful End-of-Phase 2 meeting for oral (rigosertib + azacitidine); pivotal trial ahead	☑
	Dec	3 ASH presentations including Phase 2 data for rigosertib + Aza Combination in MDS/AML	☑
2017	Q1	*INSPIRE trial enrollment update*	☐
	Q2	*Combination pivotal trial protocol review*	☐
	H2	▪ *Pre-planned interim analysis of INSPIRE trial* ▪ *Full enrollment of INSPIRE trial*	☐

Summary

- **Advanced clinical trials**
  - Phase 3 underway (IV rigosertib)
  - Phase 2 complete (Oral rigosertib)
- **Funded to deliver key 2017 milestones**
  - Oral Phase 2 to enter pivotal trial in 2017
  - IV Phase 3 interim analysis 2017; top-line data 2018
- **Underserved and growing market in MDS**
  - >10,000 patients diagnosed annually
  - No new approved therapies in over 10 years
- **Preclinical pipeline; additional business development opportunities**
- **Seasoned management team and board of directors**

Management Team

Ramesh Kumar, Ph.D.
President & CEO
Co-founder

- Bristol-Myers Squibb
- DNX
- Baxter
- Kimeragen
- Princeton University

Steven M. Fruchtman, M.D.
Chief Medical Officer

- Novartis
- Janssen
- Syndax
- Allos Therapeutics
- Spectrum Pharmaceuticals
- Mount Sinai

Mark Guerin
Chief Financial Officer

- Barrier Therapeutics
- Cardiokine
- PriceWaterhouseCoopers

Manoj Maniar, Ph.D.	Senior VP, Product Development	Alcon, SRI
Wolfgang Meyer, Ph.D.	Sr. VP Regulatory Affairs GM, Onconova GmBh	Amgen, Micromet, GPC, Fujisawa
Michael Petrone, M.D.	VP Clin. Dev. Medical Affairs and Pharmacovigilance	GSK, Roberts, GPC