ONCONOVA THERAPEUTICS

TARGETING CANCER, PROTECTING HEALTHY CELLS

BIO CEO & Investor Conference

February 13, 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.

ONCONOVA AT A GLANCE

- Founded-1998; IPO-2013 (Nasdaq: ONTX)
  - Focused on Myelodysplastic Syndromes (MDS)
- Lead clinical candidate: rigosertib
  - RAS effector pathways targeted
  - Two formulations (IV & Oral)
  - 1,100 patients treated to date
- Broad pipeline with several pre-clinical stage drug candidates
- Partnership with SymBio (Tokyo, Japan) to develop and commercialize rigosertib in Japan and Korea
  - Additional partnership discussions underway

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
- PriceWaterhouseCooper

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

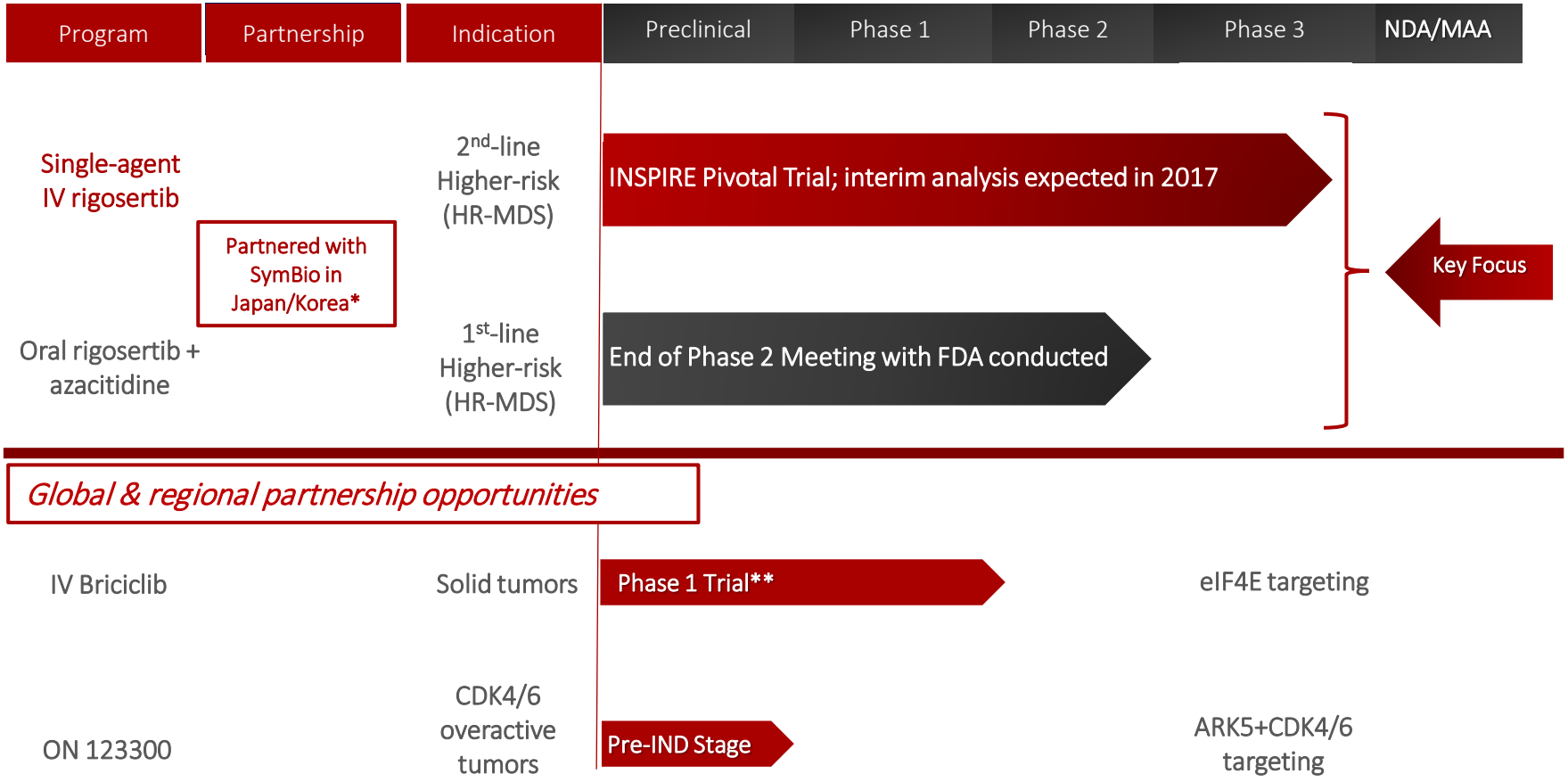
INVESTMENT HIGHLIGHTS

- Targeting underserved and growing market in Myelodysplastic Syndromes (MDS)
  - >10,000 patients diagnosed annually
  - No new approved treatments in over 10 years
- Pivotal Phase 3 Trial (INSPIRE) is underway on four continents
- Patent protection & orphan designation for MDS in the US, Europe and Japan
- Designing Phase 3 trial for Oral rigosertib, in combination with azacitidine, targeting larger front-line patient population
- Funded to deliver key 2017 milestones
  - Oral Phase 2 ready to enter pivotal trial in 2017 targeting larger patient population
  - INSPIRE (IV) Phase 3 interim analysis 2017; top-line data 2018
- Seasoned management team

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 design and review*	☐
	H2	▪ *Pre-planned interim analysis of INSPIRE trial* ▪ *Full enrollment of INSPIRE trial*	☐

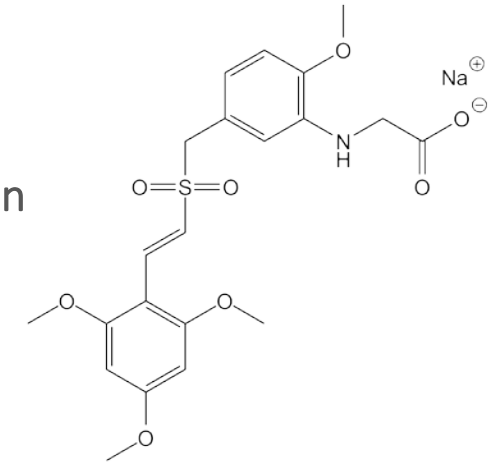
ONCONOVA CANCER PRODUCT PIPELINE



*Onconova retains rights elsewhere, including USA

**Trial on hold pending partnering and manufacturing of new product lot

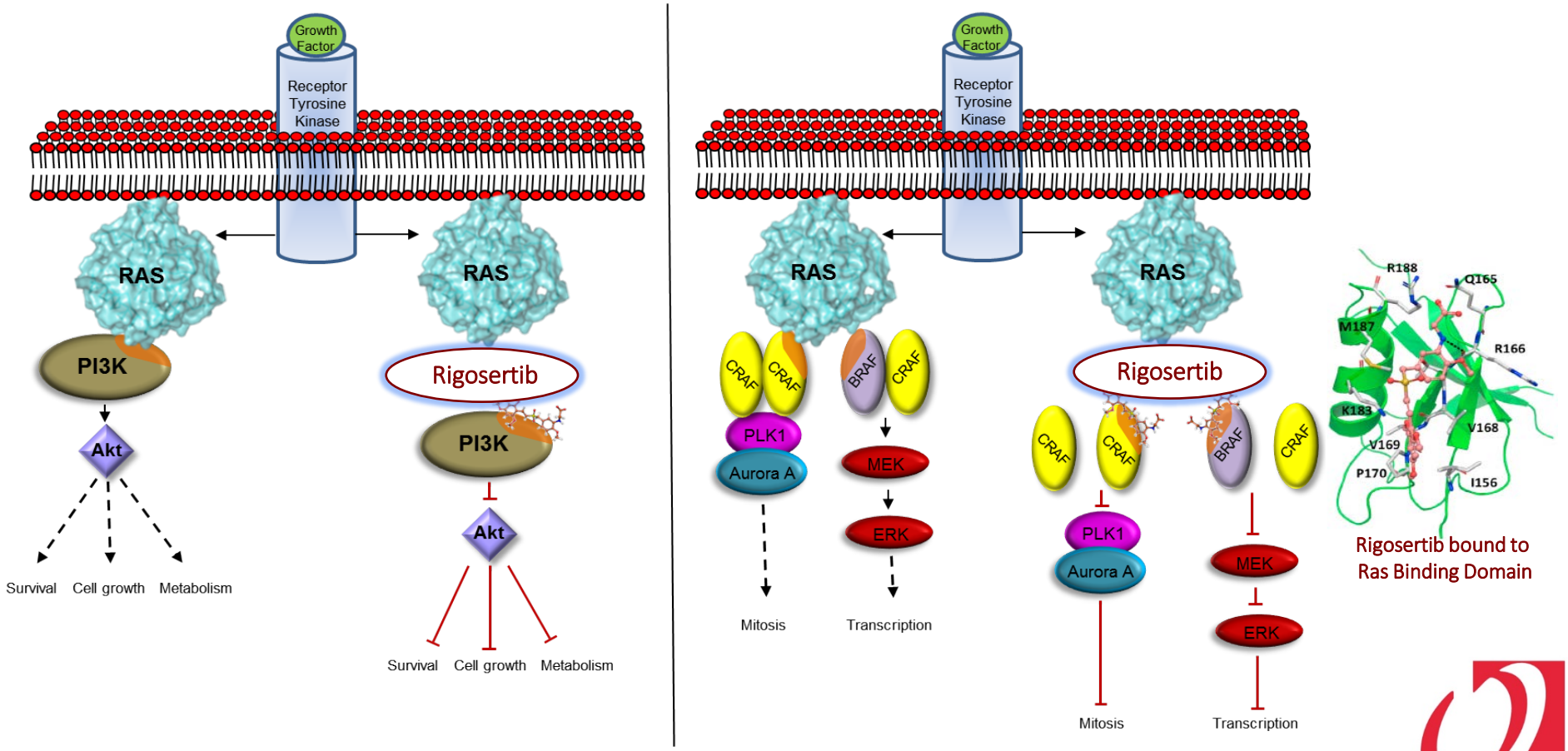
RIGOSERTIB OVERVIEW



- Rigosertib is a small molecule with a novel mechanism of action
  - Inhibits cellular signaling by blocking RAS effector pathways
  - RAS 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 oral (rigosertib + 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

NOVEL MECHANISM OF ACTION

Rigosertib blocks downstream signaling by RAS effectors including PI3K and RAF by binding to Ras Binding Domain (RBD) found in many effector proteins



Published in Cell, 2016

TWO RIGOSERTIB FORMULATIONS

IV (Phase 3 INSPIRE enrolling)

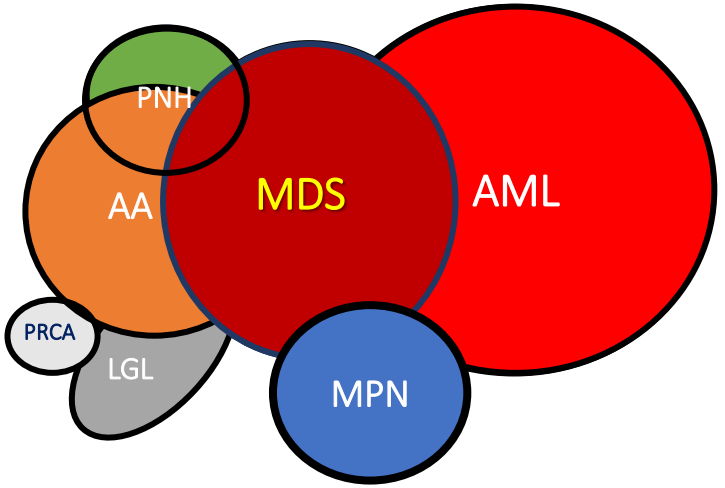
- Continuous infusion using a portable pump
- >500 patients treated in trials
- Lead indication 2nd-line HR-MDS

Oral (Phase 2 trial complete)

- Bioavailability ~35%
- >250 patients treated
- Combination with azacitidine advancing to pivotal trial in 2017

MDS OVERLAPS WITH OTHER DISEASES

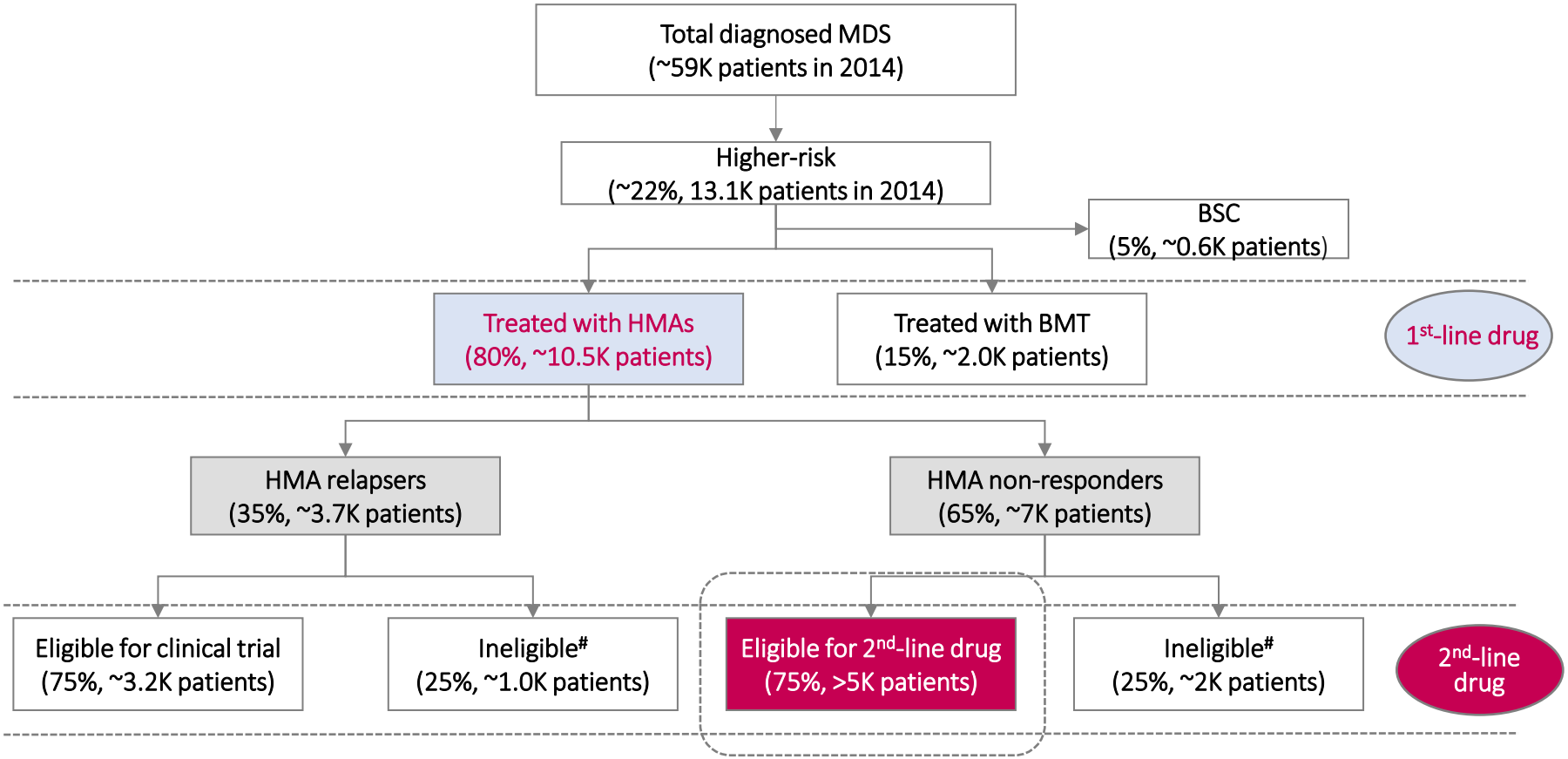
- MDS, a malignant hematopoietic stem cell disorder is characterized by:[1]
  - Bone marrow failure
  - Cytopenias
  - 30% of patients to progress to AML
- MDS has overlap with other hematological disorders
- A spectrum of risk, from low to very high, measured by IPSS-R scores.
- US prevalence estimate 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.

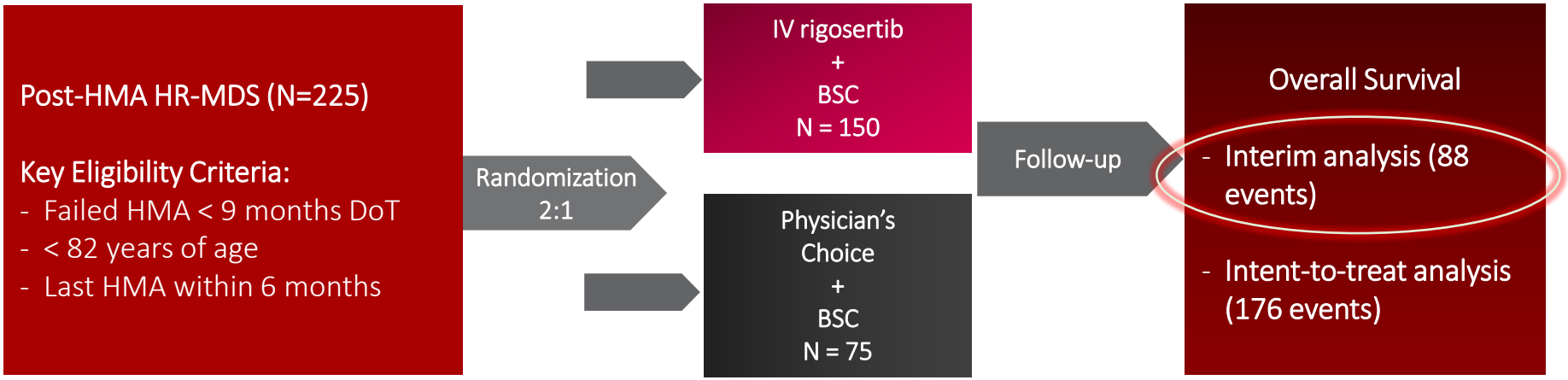
Slide credit: clinicaloptions.com

RIGOSERTIB IN HIGHER-RISK MDS



- Rigosertib is being developed for 2nd-line patients (INSPIRE Phase 3 trial)
  - no approved treatment available for these patients
- And for 1st-line patients, in combination with Azacitidine, the current standard of care

INSPIRE: GLOBAL PHASE 3 TRIAL



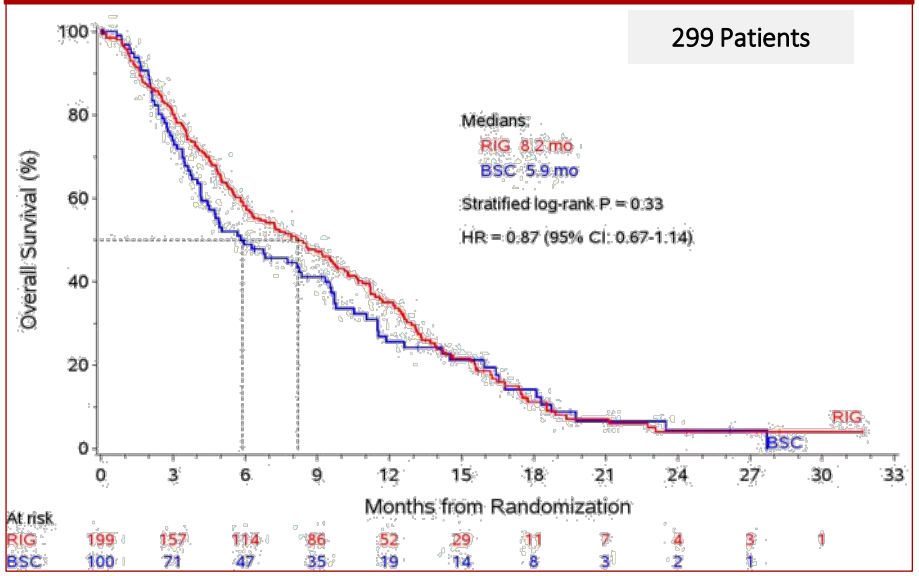
- Statistical analysis: two analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Trial can succeed in two ways: ITT population or IPSS-R Very High Risk
- Genomic sequencing of patient samples

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

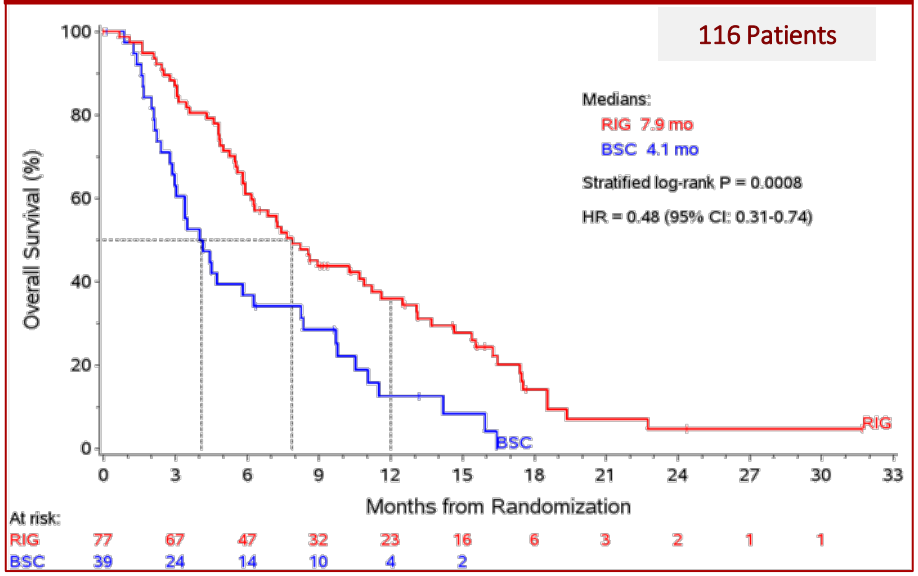
PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

Data from ONTIME paper* published in *Lancet Oncology*

ITT for ONTIME Trial



Subpopulation for INSPIRE Trial (ONTIME subset)



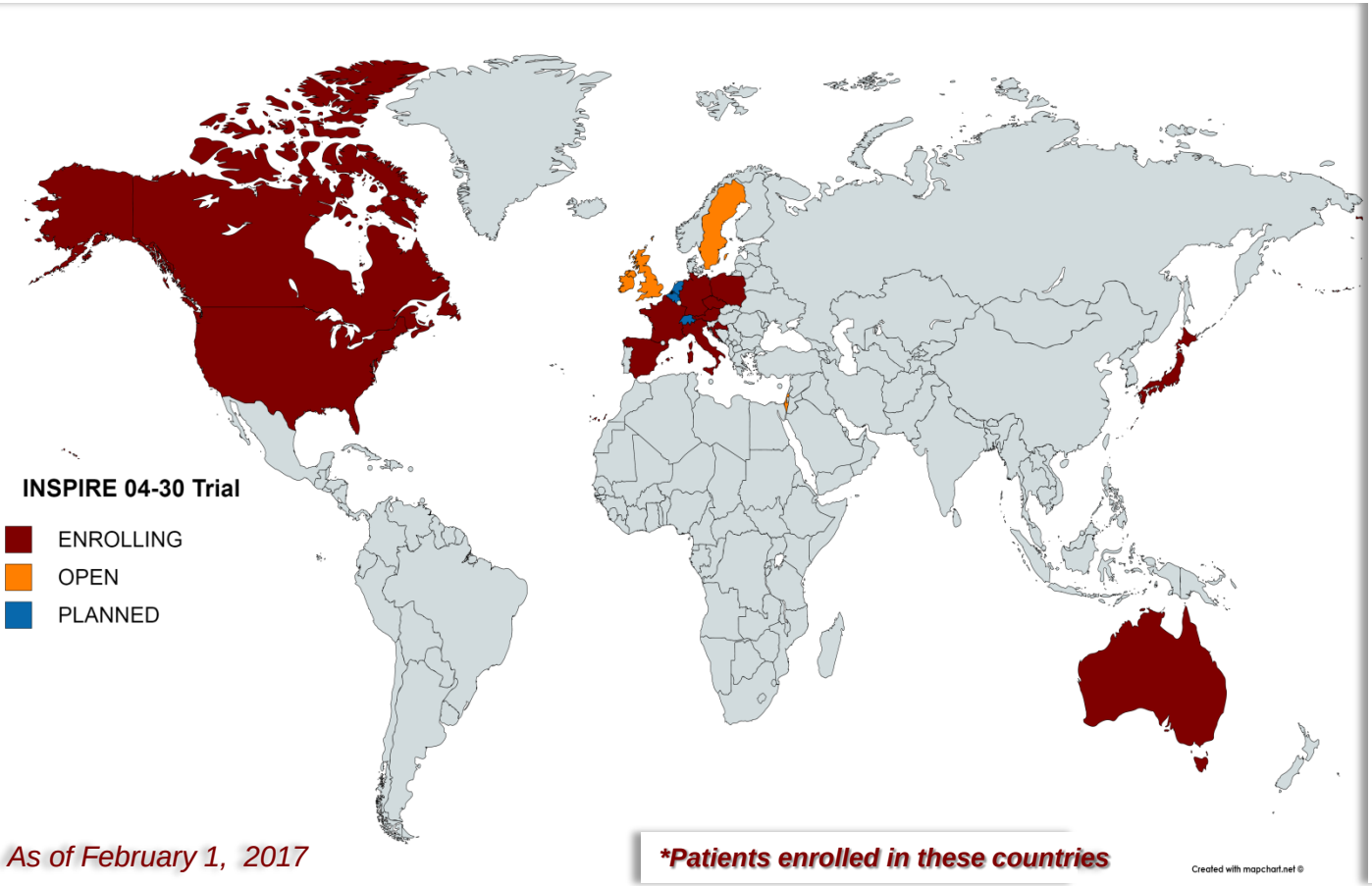
ITT OS analysis of ONTIME – HR= 0.87; NS survival benefit

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

GLOBAL INSPIRE TRIAL PROGRESS

*The **IN**ternational **S**tudy of **P**hase III **IV** **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.*



As of February 1, 2017

***Patients enrolled in these countries**

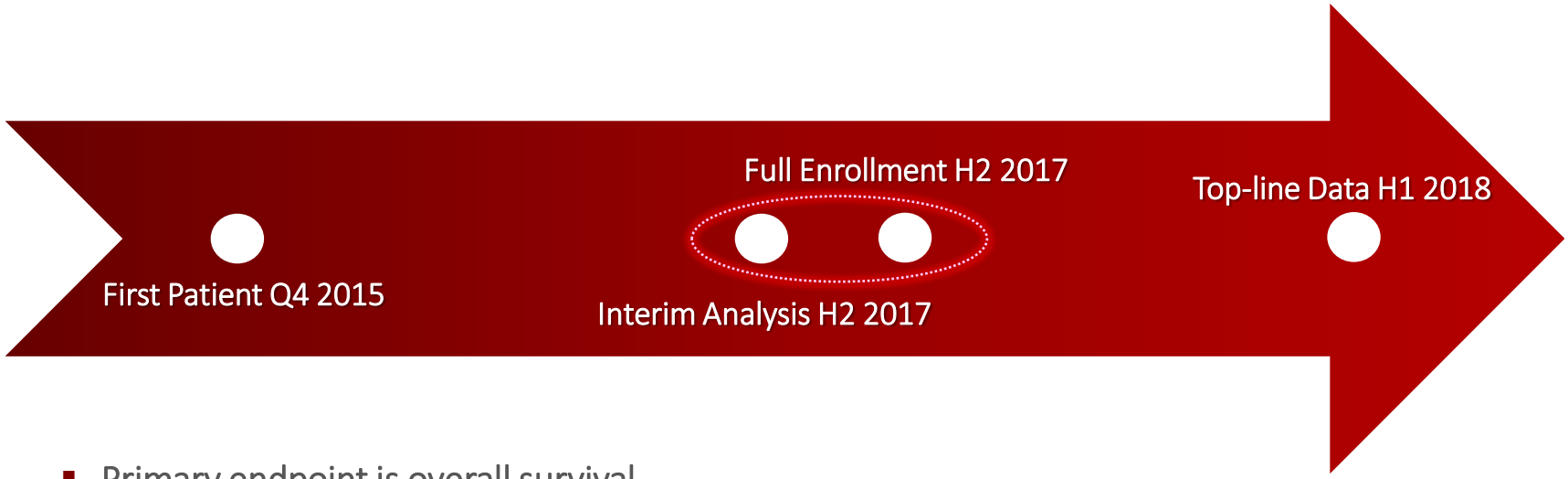
Country	Sites
1. USA*	43
2. Japan*	32
3. Spain*	12
4. Israel	10
5. France*	9
6. Italy*	9
7. Germany*	8
8. Canada*	6
9. Poland*	6
10. U.K.	5
11. Australia*	5
12. Belgium	5
13. Czech Rep.*	5
14. Ireland	4
15. Sweden	4
16. Croatia*	4
17. Austria*	3
18. Netherlands	2
19. Switzerland	2

225 patients to be enrolled

- **Target: 174 sites selected in 19 countries on 4 continents**
  - **Currently 143 sites activated in 16 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

EPIGENETIC AND GROWTH FACTOR PATHWAY MUTATIONS SYNERGIZE IN INDUCING LEUKEMIC TRANSFORMATION

Preclinical/clinical evidence suggest that combination of epigenetic therapy plus growth factor signaling inhibitor could be effective in curbing MDS pathogenesis

Complexity of MDS

- Defined by IPSS-R categories
- Certain karyotypes
- Different types of mutations
- Sequential progression

DNA methylation changes

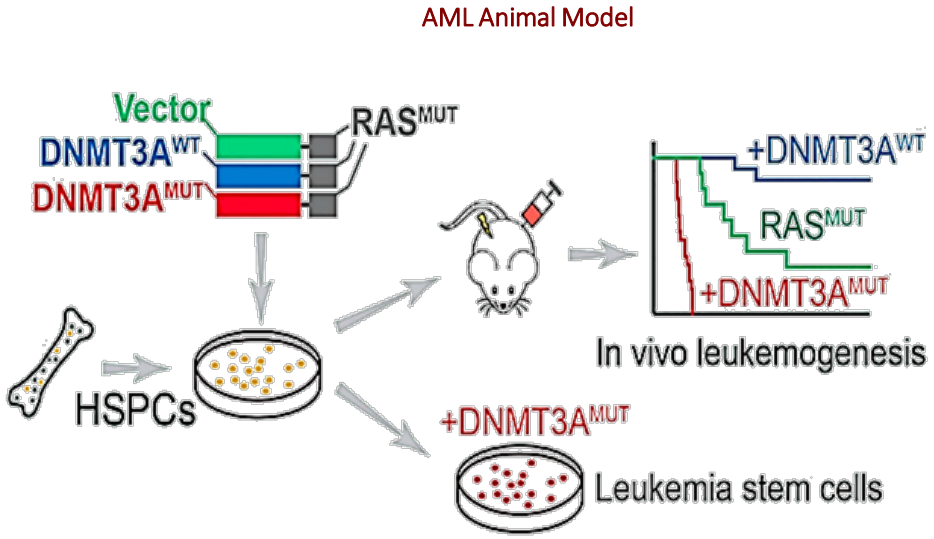
- Addressed by HMA inhibitors
- Early (lower-risk) stage

Signal transduction changes

- Later stage mutations
- May be addressed by rigosertib

Combination approach

- Address more molecular defects
- May improve outcomes in more patients



Lu et al., 2016 *Cancer Cell*

UPDATED 09-08 PHASE 2 TRIAL RESULTS

Combination oral Rigosertib + Azacitidine in MDS patients

Included a diverse patient population including

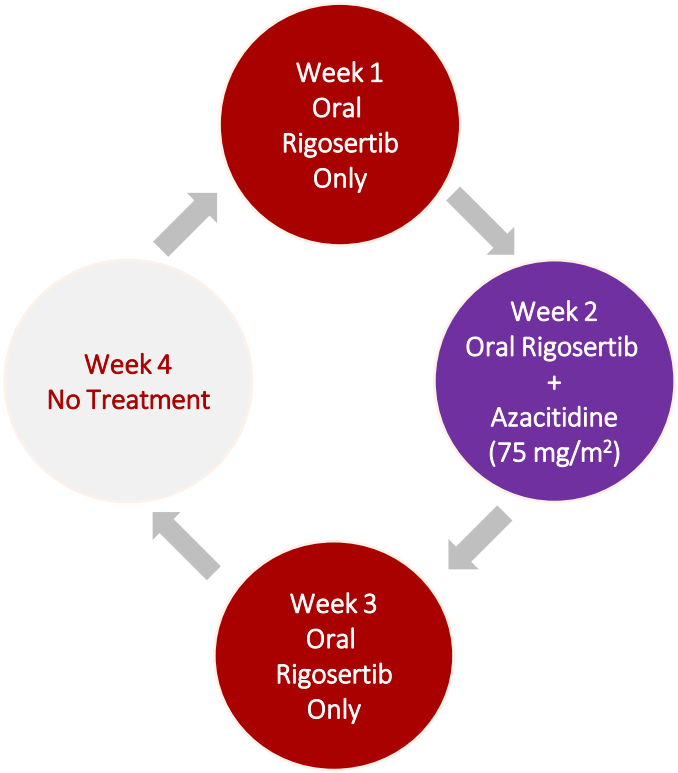
- HMA-naïve front-line patients
- HMA pre-treated second-line patients
- AML patients

Phase 2 dose: 560 mg qAM, 280 mg qPM

- Oral rigosertib twice daily on Day 1-21 (28-day cycle
- Azacitidine 75 mg/m2/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



EFFICACY RESULTS FOR COMBINATION TRIAL

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%

NEXT STEPS FOR RIGOSERTIB + AZACITIDINE DEVELOPMENT

- **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%)
  - Overall response rate of 62% in 13 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 in 1st line MDS

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
Regulatory Path	To be explored	Special Protocol Assessment (SPA), Fast-track etc.
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*

IP SUMMARY

- Onconova portfolio contains only New Chemical Entities (NCEs)
  - All NCEs are patent protected for composition of matter and other claims
- Rigosertib (ON 01910.Na) covered by issued US and other patents
  - Earliest to expire composition claim valid until 2026
  - Potential for Hatch-Waxman extensions
  - Composition of rigosertib combination with azacitidine expires 2028
  - Single digit royalty to Temple University
- Orphan designation granted in US, Europe & Japan for rigosertib in MDS
- Issued US and foreign patents cover the rest of the pipeline
  - Briciclib, Recilisib are in in Phase 1
  - ON 123300 (ARK5+CDK4/6 inhibitor) in advanced preclinical stage

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	LifeSci Capital; Maxim; SeeThru Equity; Van Leeuwenhoeck Research
Debt	0
Liquidity	▪ $ 17.4 million gross proceeds from rights offering in July 2016 ▪ Cash and cash equivalent of $25.8 million*
Burn-rate	$5.7 million for Q3-2016*
Partnerships	Rigosertib is partnered with SymBio Pharmaceuticals in Japan/Korea Onconova retains rights to the rest of the world
**As per Q3 2016 financials*	

BOARD OF DIRECTORS

Michael B. Hoffman Chairman	Partner, Riverstone Holdings LLC
Henry S. Bienen Ph.D.	Served as the 15th President of Northwestern University
Jerome E. Groopman M.D.	Chief of Experimental Medicine at the Beth Israel Deaconess Medical Center, Harvard
Ramesh Kumar Ph.D.	President and CEO, Onconova Therapeutics Inc., co-founder
Viren Mehta Pharm.D.	Managing Member of Mehta Partners
E. Premkumar Reddy Ph.D. Co-founder, Lead Scientific Advisor	Professor in the Department of Oncological Sciences & Department of Structural & Chemical Biology at the Mount Sinai School of Medicine
James J. Marino, Esq.	Former partner at Dechert LLP
Jack Stover	CEO, Interpace Diagnostics; former partner PwC

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Anna Marie Skalka, Ph.D.	Fox Chase Cancer Center
George F. VandeWoude, Ph.D.	Van Andel Research Institute
Peter K. Vogt, Ph.D.	The Scripps Institute

SUMMARY

- Advanced clinical trials
  - Phase 3 underway (IV rigosertib)
  - Phase 2 complete (Oral rigosertib)
- Funded to deliver key 2017 milestones
  - Oral Phase 2 ready 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

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ir@onconova.us