

Corporate Update

July 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 in 2013 (Nasdaq: ONTX)
- Lead clinical candidate: rigosertib
 - Targets RAS effector pathways (Cell, 2016)
 - Two formulations (IV & Oral)
 - Focused on Myelodysplastic Syndromes (MDS)
 - 1,200+ patients treated in clinical trials for MDS and other conditions
- Broad pipeline with several pre-clinical stage drug candidates
- Partnership Since 2011 with SymBio in Japan and Korea
 - Additional partnerships sought

Key milestones upcoming in H2-2017 and 2018

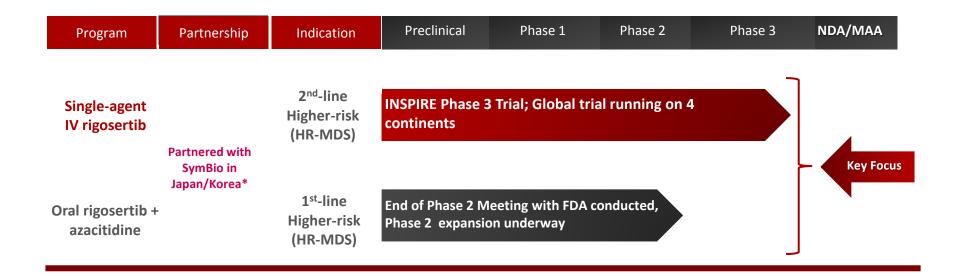


ONCONOVA HIGHLIGHTS

- Targeting underserved market in Myelodysplastic Syndromes (MDS)
 - >10,000 patients diagnosed annually in the U.S. with Higher-risk (HR) MDS
 - No new approved treatments in over 10 years
- Phase 3 Trial (INSPIRE) underway on 4 Continents for 2nd line HR-MDS
- Patents & Orphan Designation for MDS in the US, Europe and Japan
- Rigosertib partnered with SymBio in Japan/Korea
- Designing Phase 3 trial for Oral rigosertib + azacitidine combination
 - Targeting larger first-line patient population for higher risk MDS
- Funded to deliver key 2017 milestones
 - INSPIRE (IV) Phase 3 interim analysis 2017
 - Top-line Phase 3 data in 2018
- Pipeline assets beyond rigosertib available for partnerships

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ONCONOVA MDS PIPELINE

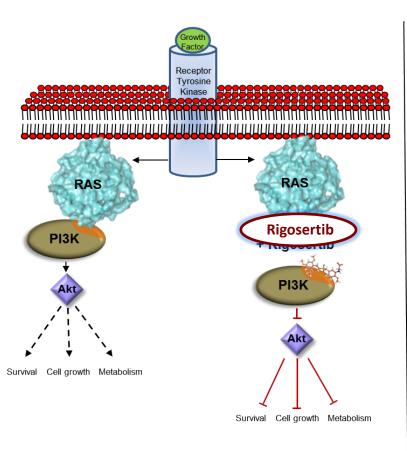


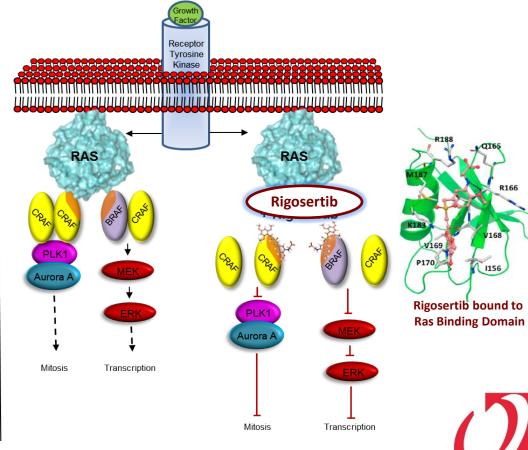
- More than 700 MDS patients have been treated in rigosertib Phase 1-3 trials
 - IV and Oral rigosertib, plus oral rigosertib combination with azacitidine
- Includes, in addition to Higher Risk MDS, Lower Risk, transfusion dependent patients
- New data on IV rigosertib:
 - Phase 2b 04-24 trial results presented at ASCO 2017
 - Interim analysis of INSPIRE study expected in H2-2017
 - Top-line analysis of INSPIRE in 2018



NOVEL MECHANISM OF ACTION

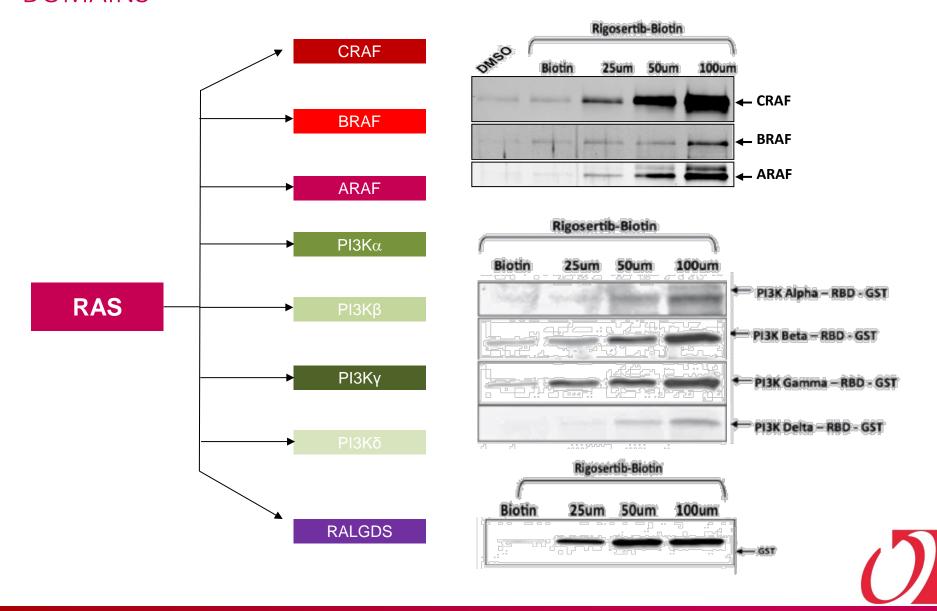
Rigosertib is believed to block downstream signaling by RAS effectors including PI3K and RAF by binding to Ras Binding Domain (RBD) found in many effector proteins





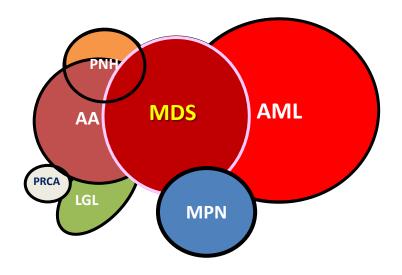
Published in Cell, 2016

RIGOSERTIB BINDS TO MULTIPLE RAS EFFECTOR RAS BINDING DOMAINS



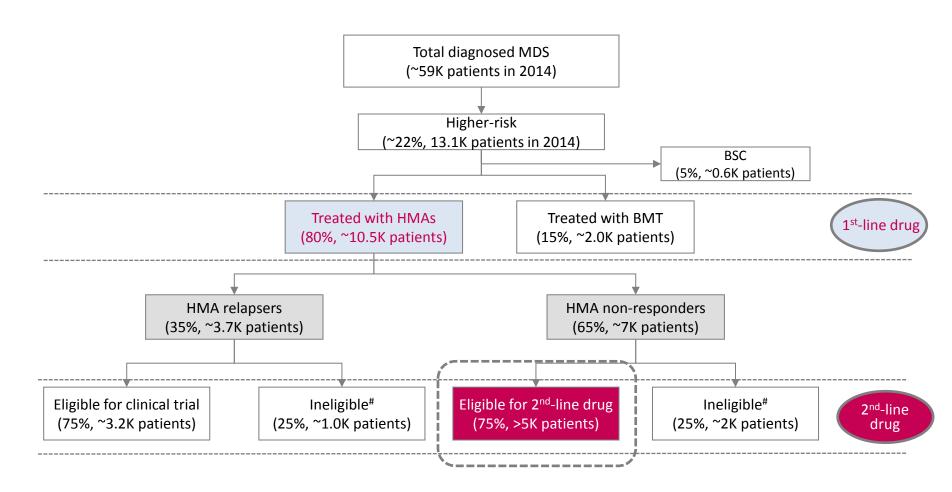
MDS OVERLAPS WITH OTHER DISEASES

- MDS, a malignant hematopoietic stem cell disorder characterized by:^[1]
 - Bone marrow failure
 - Cytopenias
 - 30% of patients progress to AML
- 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





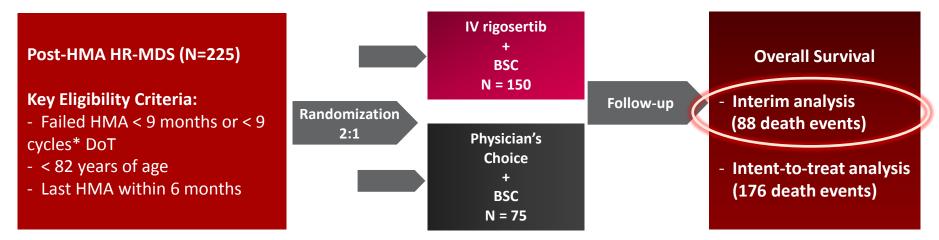
RIGOSERTIB IN HIGHER-RISK MDS



- Rigosertib is being developed for 2nd-line patients (INSPIRE Phase 3 trial)
- And for 1st-line patients, in combination with Azacitidine, the current standard of care



INSPIRE: GLOBAL PHASE 3 TRIAL



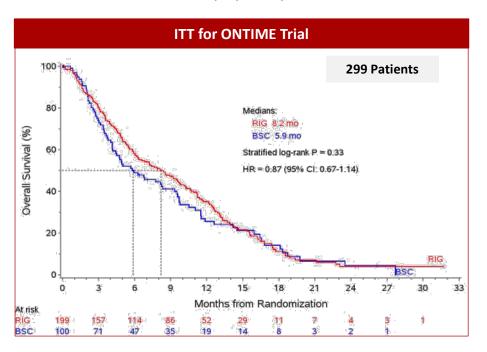
^{*9} cycles within 12 months of starting treatment

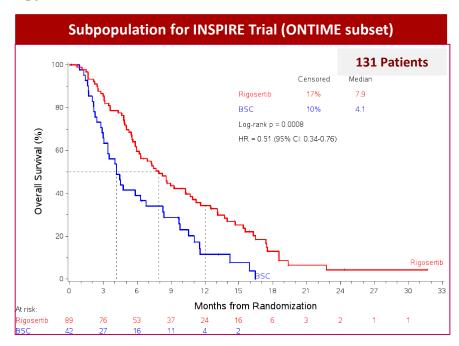
Commentary on new trial in recent publication: Emilio P Alessandrino, Matteo G Della Porta. Novel trial designs for high-risk myelodysplastic syndromes; The Lancet Oncology 2016 (17): 410–412



PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

Data from ONTIME paper* published in Lancet Oncology





ITT OS analysis of ONTIME – HR= 0.87; NS survival benefit ITT OS of proposed INSPIRE population – HR = 0.51; P = 0.0008

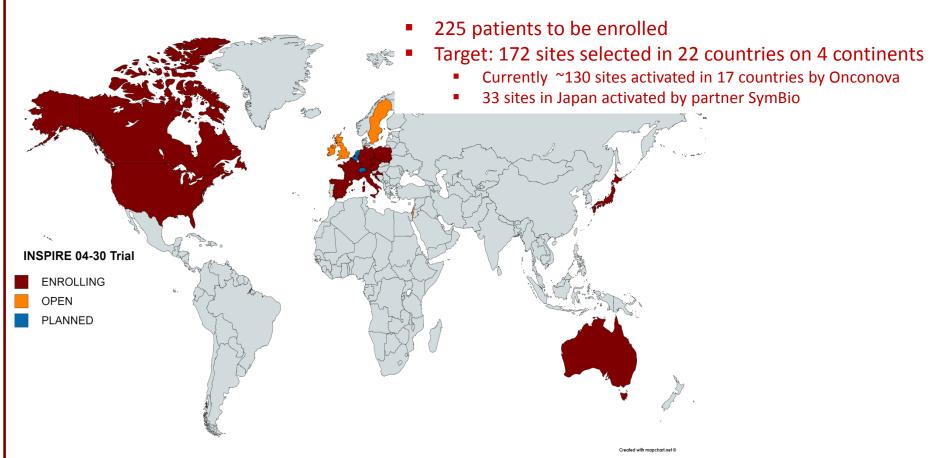
*Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, et al. Rigosertib versus best supportive care for patients with higher-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, Phase 3 trial;

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, designed following feedback 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.



Latest guidance (May 15 earnings call):

- Interim analysis on track for H2-2017
- Enrollment rate indicating full accrual in Q1-2018
- Top-line analysis in 2018



INSPIRE: KEY OPINION LEADERS PARTICIPATING IN THE PHASE 3 TRIAL

ONTIME participants in red (highest accruing sites in bold)
Sites in Japan not included in this list

Sites in USA

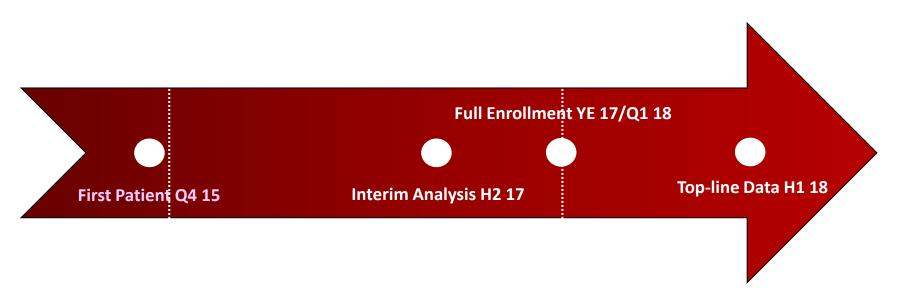
- Maria R. Baer, MD University of Maryland Greenebaum Cancer Center, Baltimore
- Robert H. Collins, Jr., MD, FACP University of Texas Southwestern Medical Center, Dallas
- Guillermo Garcia-Manero, MD University of Texas MD Anderson Cancer Center, Houston*
- Lucy Godley, MD, PhD University of Chicago Comprehensive Cancer Center, Chicago
- Aref Al-Kali, MD Mayo Clinic Rochester, Minnesota
- Gail J. Roboz, MD Weill Medical College of Cornell University New York Presbyterian Hospital, New York
- Bart Scott, MD Fred Hutch Cancer Center, Seattle, Washington
- Jamile Shammo, MD Rush University Medical Center, Chicago
- Lewis R. Silverman, MD Icahn School of Medicine at Mount Sinai, New York**
- Selina Luger, MD University of Pennsylvania Cancer Center, Philadelphia
- Rafael Bejar, MD, PhD Moores Cancer Center at the University of California, San Diego
- Christopher R. Cogle, MD University of Florida Shands Hospital, Gainesville
- Azra Raza, MD Columbia University Medical Center, New York

First* & senior** author in Lancet Oncology, 2016 paper on ONTIME results

Sites in Europe, Israel and Australia

- Pierre Fenaux, MD, PhD Hôpital St Louis/ Université Paris, France
- Norbert Vey, MD Institut Paoli- Calmettes, Marseille, France
- Aristotle Giagounidis, MD, PhD St. Johannes Hospital Heinrich-Heine Universität, Duisburg, Germany
- Detlef Haase, MD, PhD Georg-August- Universität Göttingen, Göttingen, Germany
- Uwe Platzbecker, MD Universitätsklinikum Carl Gustav Carus, Dresden, Germany
- Valeria Santini, MD University of Florence Azienda OSP Careggi, Florence, Italy
- María Díez-Campelo, MD, PhD Hospital Universitario de Salamanca, Salamanca, Spain
- Guillermo F. Sanz, MD Hospital Universitario La Fe, Valencia, Spain
- Jaroslav Cermák, MD, PhD Institute of Hematology and Blood Transfusion, Prague, Czech Republic
- Eva Hellstrom-Lindberg, MD, PhD Karolinska Institutet, Karolinska, Sweden
- Ghulam J. Mufti, DM, FRCP, FRCPath King's College London & King's College Hospital, London, UK
- Moshe Mittelman, MD Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel
- Michael Pfeilstöcker, MD Hanusch Hospital Medical Univ of Vienna, Vienna, Austria
- Jake Shortt, MD Monash Health, Monash Medical Centre, Melbourne, Victoria, Australia
- Arjan A. van de Loosdrecht, MD, PhD Vrije Universiteit Medical Center, Amsterdam, The Netherlands

TIMELINES FOR DATA ANALYSIS FOR INSPIRE 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
 - Dual primary endpoints: Overall survival in ITT population or IPSS-R Very High Risk
- Exploratory genomic sequencing of patient samples

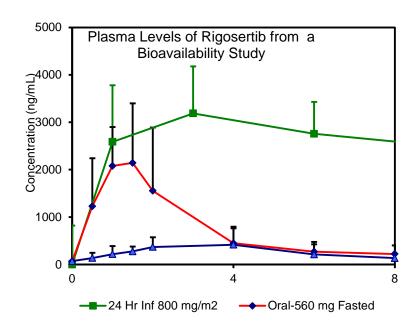


TWO RIGOSERTIB FORMULATIONS

- IV (Phase 3 INSPIRE ongoing)
 - Continuous infusion using a portable pump
 - >500 patients treated in trials
 - Lead indication 2nd-line HR-MDS

- Oral (Phase 2 enrolled)
 - Bioavailability ~35%
 - >200 patients treated
 - Combination with azacitidine for HR-MDS and AML









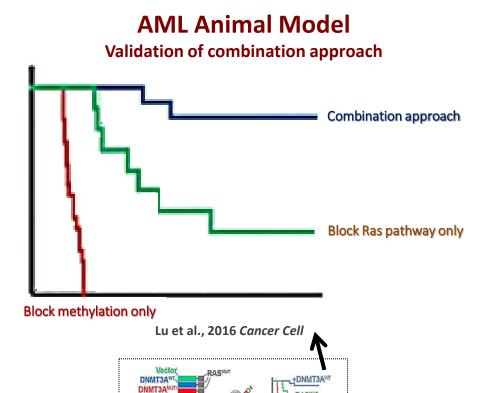
MECHANISTIC RATIONALE FOR COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

Preclinical evidence supports synergism of rigosertib + azacitidine combination

- Complexity of MDS
 - Defined by IPSS-R categories
 - Certain karyotypes
 - Different types of mutations
- DNA methylation changes
 - Addressed by HMA inhibitors
 - Early stage events
- Signal transduction changes
 - Later stage mutations
 - May be addressed by rigosertib
- Combination approach

July 2017

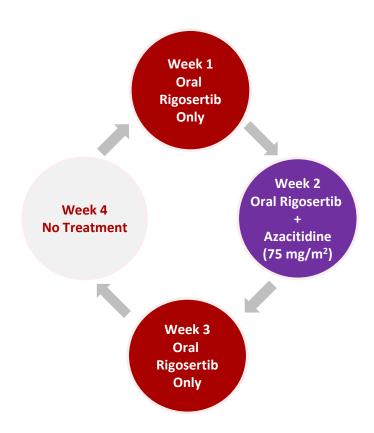
- Addresses more molecular defects
- Potential for synergistic activity



COMBINATION THERAPY PHASE 1/2 TRIALS

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





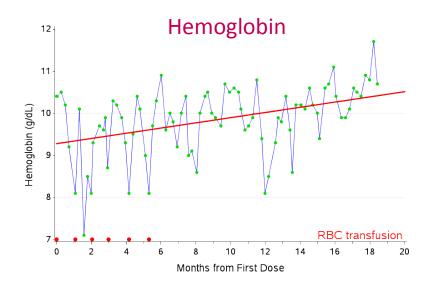
EFFICACY RESULTS FOR COMBINATION TRIAL

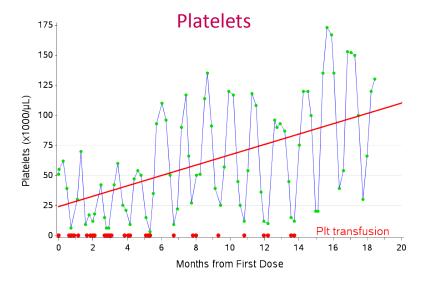
	Response per IWG 2006				
Response Criteria	Overall evaluable (N=33)	No prior HMA (N=20)	HMA resistant (N=13)		
Complete Remission*	8 (24%)	7 (35%)	1 (8%)		
Marrow CR + Hematologic Improvement (HI)	10 (30%)	6 (30%)	4 (31%)		
Marrow CR alone	6 (18%)	3 (15%)	3 (23%)		
Hematologic Improvement alone	1 (3%)	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

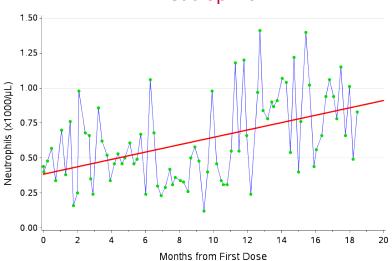


HEMATOLOGY TRENDS FOR PATIENT 101-006









- 12 cycles of AZA stable disease
- RBC and platelet transfusions
- Blasts 7%
- Monosomy 7
- Runx-1
- AZA + RIG in 09-08 for 20+ months
- Complete remission
- RBC transfusion independent
- <5% blasts</p>
- PB CR criteria



KEY SAFETY DATA FROM RIGOSERTIB COMBINATION TRIAL (STUDY 09-08)

Azacitidine Package Insert¹

Oral Rigosertib + Aza

Adverse Event	Grade ≥3	Adverse Event	Grade ≥3
Haematuria	2.3%	Haematuria	7.0%
Anemia	13.7%	Anemia	0
Neutropenia	61.1%	Neutropenia	19.0%
Thrombocytopenia	58.3%	Thrombocytopenia	27.0%

- Rigosertib + azacitidine generally well tolerated
 - 4/37 MDS patients withdrew due to AE
 - 2/37 MDS patients had dose reduction
- Safety profile of combination did not differ from reported toxicities of azacitidine alone



¹http://www.vidaza.com/pi.pdf

NEXT STEPS FOR RIGOSERTIB + AZACITIDINE DEVELOPMENT

Key Parameters and Milestones for Oral Rigosertib + Azacitidine Phase 3 Program							
Phase 3 Design	Phase 3 Design Randomized Controlled 1:1 randomization between Aza + placebo and Aza + oral rigosertib						
Patient Population	First-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					

Current activities:

- Phase 2 trial expanded
 - Up to 40 more patients
 - Dose and schedule optimization
 - Gain additional efficacy data
- Phase 3 protocol synopsis created
- Scientific advice sought from EMA
- FDA Special Protocol Assessment process to start after completing EMA process
 - Expected to be completed in 2017



OVERVIEW OF SAFETY

- Over 1,180 patients treated with rigosertib in 27 Phase 1-3 trials
 - MDS/other hematologic malignancies (N = 672)
 - advanced cancer/solid tumors (N = 508) were treated in 27 Phase 1-3 clinical trials
- No treatment emergent myelosuppression, cardiotoxicity, or neurotoxicity
 - Minimal myelosuppression by rigosertib might represent a distinct advantage given the compromised bone marrow function of patients with MDS
- Generally, no need for premedication during the studies
- Potential safety signals are being monitored on an ongoing basis
- Next Investigator Brochure and Development Safety Update Report : July 2017



RIGOSERTIB IP SUMMARY

- 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 earliest expiry 2028
 - Single digit royalty to Temple University
- Orphan designation granted in US, Europe and Japan for rigosertib in MDS
- Efforts directed to obtaining additional coverage
 - Formulation patent filed as a provisional application
 - Potential to seek patent coverage for administration schedule, process etc.

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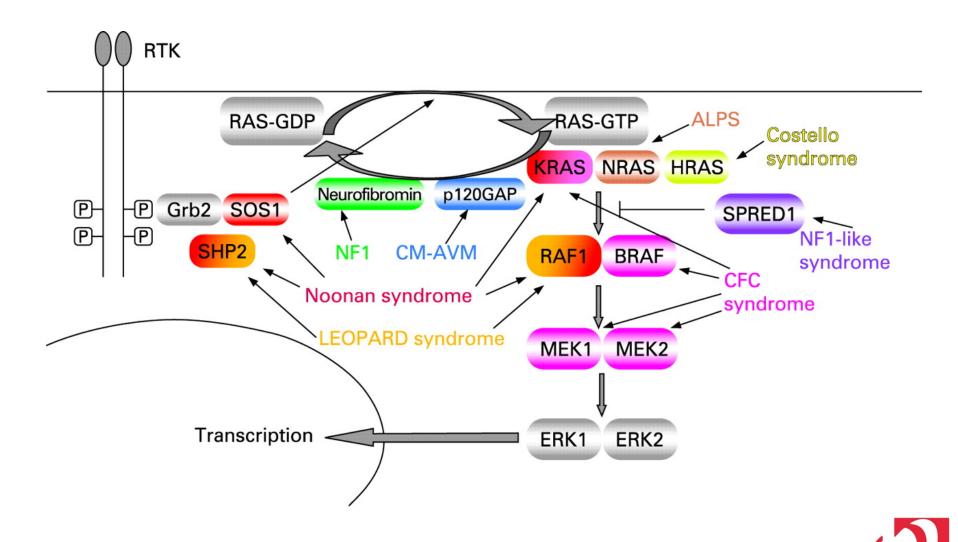
RIGOSERTIB IS PARTNERED IN JAPAN/KOREA SINCE 2011



Partnerships sought in other territories



RASOPATHIES: CAUSATIVE MUTATIONS NOT LIMITED TO RAS





ONCONOVA PRODUCT CANDIDATE PIPELINE

Not including Rigosertib

- Patent protected, differentiated small molecule compounds
- Partnerships sought for all programs

Compound	Target	Stage	Next Step	Competition	Patents
Briciclib	eIF4E (Cyclin D)	Phase I*	Phase II Dose	4EGI-1	Issued US
Recilisib	GSK-3, Akt	Phase I	Primate efficacy	CBLB502	Issued WW
ON 123300**	CDK4/6; ARK5	Preclinical	Toxicology	Palbociclib	Issued US, EP
ON 150030**	FLT3 + Src	Pre-clinical	Animal studies	Dasatinib	In process
ON 1231320	PLK2	Formulation	Pre-IND	Volasertib	Issued
ON 108600	CK2	Formulation	Pre-IND	CX-4945	Issued
ON 146040	PI3K a/d	Pre-clinical	Toxicology	IPI-145	In process

^{*}On hold, pending new drug product



^{**}New data presented at 2017 AACR conference

MULTIPLE CDKS & CELL CYCLE INHIBITORS*

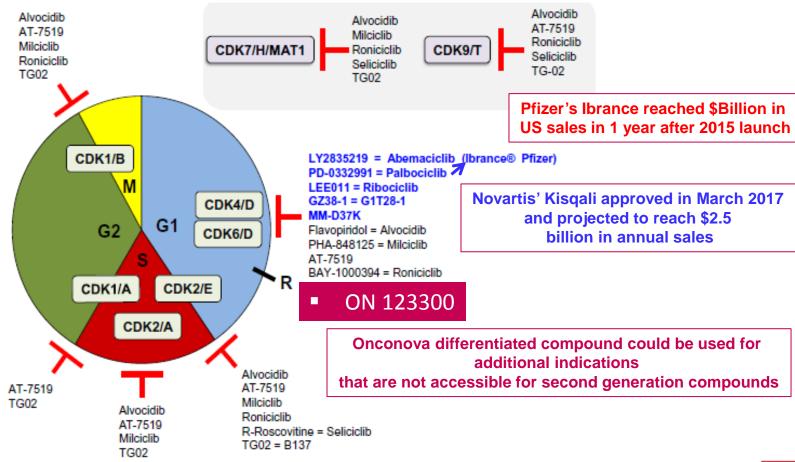
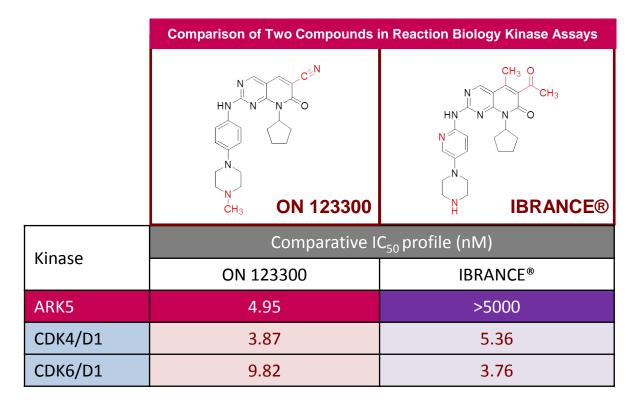


Figure 5. Cell cycle and transcription regulation CDK inhibitors under clinical evaluation. Specific CDK4 and CDK6 inhibitors are indicated in blue.



DIFFERENTIATED KINASE INHIBITION THROUGH TARGETING OF ARKS



Reddy MVR et al., Journal of Medicinal Chemistry 2014 57 (3), 578-599



FINANCIAL DETAILS

Onconova founded in 1998; public since 2013

Ticker	Nasdaq ONTX
Stock information	 9.9 million shares Public float >84% 52-week range \$1.85 - \$4.99 Average daily volume 114,000
Ownership*	Tyndall, Tavistock, Sabby, Shire; insiders including management
Analyst coverage	Laidlaw, Maxim, LifeSci Advisors, Van Leeuwenhoeck Research (VLR), SeeThru Equity
Debt	\$0
Liquidity	 Cash and cash equivalents of \$15.4 million* Funded to deliver key milestones in 2017
Burn-rate	Average \$5.6 million per quarter over the last 4 quarters
Partnerships	Rigosertib is partnered with SymBio Pharmaceuticals in Japan/Korea Onconova retains rights to the rest of the world

^{*}As of 3-31-2017 (fund raise of ~\$6 million gross in April/May 2017)





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	

SUMMARY

- Advanced clinical trials
 - Phase 3 underway (IV rigosertib)
 - Phase 2 complete (Oral combination rigosertib)
- Funded to deliver key 2017 milestones
 - Oral Phase 2 ready to enter Phase 3 trial in 2017 with additional funding
 - 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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BACK-UP SLIDES



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



ADVISORY BOARD

Ross C. Donehower, M.D.	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
James F. Holland, M.D.	Mount Sinai School of Medicine
Stephen Nimer, M.D.	Sylvester Cancer Center at the University of Miami Hospitals and Clinics
David R. Parkinson, M.D.	Venture Partner at NEA
Alan R. Williamson, Ph.D. Chairman	Retired Merck and Glaxo pharmaceutical executive; former Abingworth
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



KEY PARAMETERS OF INSPIRE TRIAL

- A 2:1 random assignment ratio; 225 patients total
- Type 1 error $\alpha = 0.04$ using a 2-sided log-rank test
 - Primary endpoint of overall survival in the intention-to-treat population
 - Exponential distribution of survival on treatment groups with constant death rate
- Type 2 error β = 0.20 (80% power)
- Expected mOS of 4.5 (control) and 7.2 months (rigosertib) groups
 - Target hazard ratio of 0.625
- An interim look for futility after the observation of 50% of deaths on both arms
- A uniform accrual period of 24 months
 - An additional follow-up period of 6 months after the last patient is randomized



REVISED IPSS: PROGNOSTIC SCORE VALUES AND RISK CATEGORIES/SCORES

Prognostic	Prognostic Score Value						
Variable	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

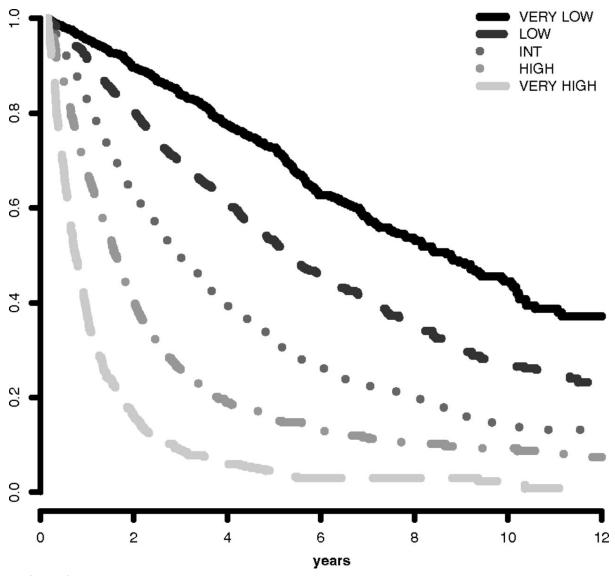
Greenberg PL, et al. Blood. 2012;120:2454-2465.

Slide credit: clinicaloptions.com



July 2017

REVISED IPSS-R IN RELATION TO SURVIVAL



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



IPSS-R RISK AND CLINICAL OUTCOME FOR FRONT-LINE PATIENTS

7012 patients, at diagnosis, on Best Supportive Care

Parameter	Very Low	Low	Intermediate	High	Very High
IPSS-R score	<=1.5	>1.5-3	>3-4.5	>4.5-6	>6
Patients^ (%)	19	38	20	13	10
Survival, years***	8.8	5.3	3.0	1.6	0.8
Median months to 25% of patients in AML	NR	10.8	3.2	1.4	0.7
ONTIME Study (%) 15% were "unknown"	0	0	9	31	45

Median survival of VHR patients on BSC arm in the ONTIME study was 3.2 months

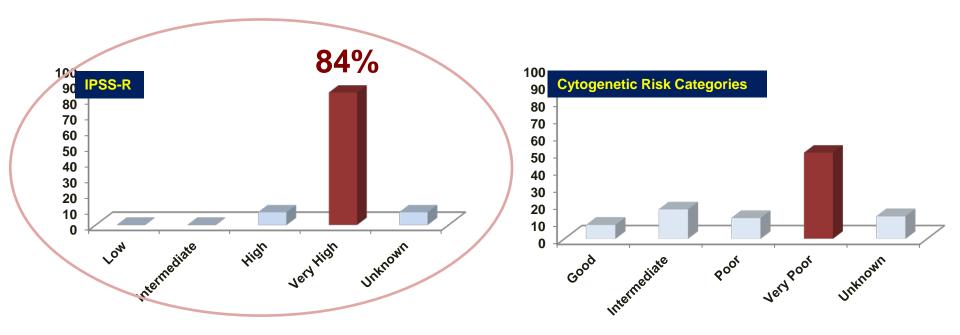


^{***}Medians, years ^Median time to 25% AML evolution

^{*}Greenberg, Tuechler, Schanz et al, Revised International Prognostic Scoring System (IPSS-R) for Myelodysplastic Syndrome, Blood 120: 2454, 2012.

^{**}Schanz J et al, J Clin Oncology 2012; 30:820

DISTRIBUTION (%) OF TP53 MUTATIONS BY PROGNOSTIC RISK CLASSIFICATION



- 100% of Monosomy 7 and Trisomy 8 patients tested carried one or more myeloid mutations
- Older patients (>80 years) had fewer TP53 mutations
- Complex karyotype patients had more mutations

