ONCONOVA
THERAPEUTICS
TARGETING CANCER, PROTECTING HEALTHY CELLS

2017 Pioneers Conference

May 2, 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

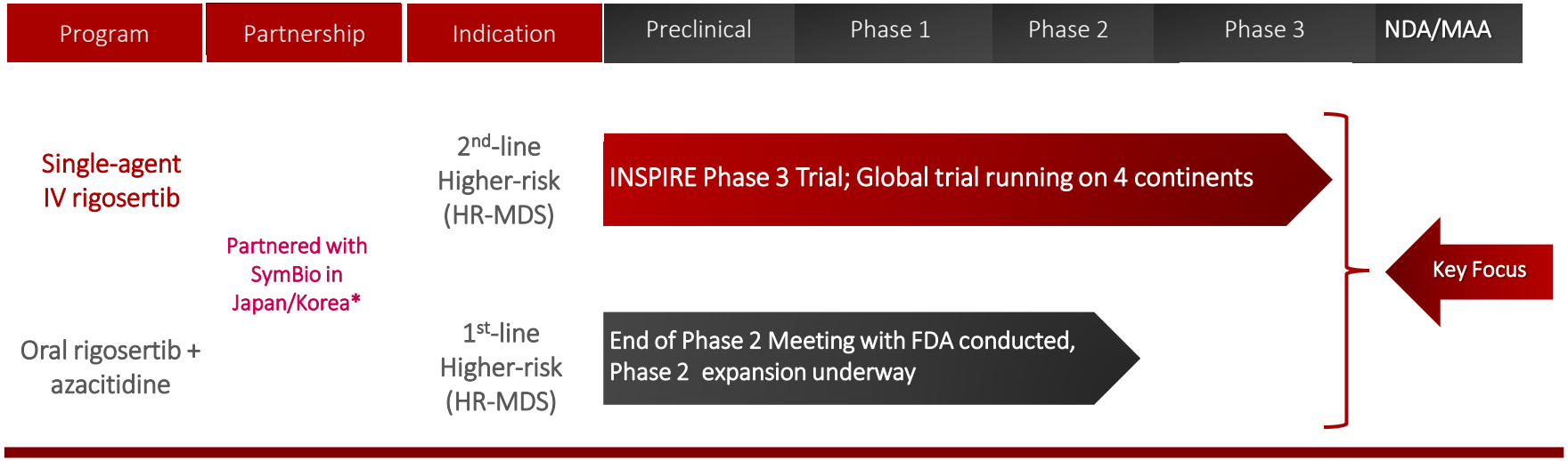
FINANCIAL DETAILS

Onconova founded in 1998; public since 2013	
Ticker	Nasdaq ONTX
Stock information	▪ 9.5 million shares ▪ Public float >80% ▪ 52-week range $2.04 - $6.87 ▪ Average daily volume 130,000
Ownership*	Tyndall, Tavistock, Sabby, Shire; insiders including management
Analyst coverage	Laidlaw, Maxim, Van Leeuwenhoeck Research (VLR), SeeThru Equity, LifeSci Advisors
Debt	$0
Liquidity	▪ Cash and cash equivalents of $21.4 million* ▪ Funded to deliver key milestones in 2017
Burn-rate	$5.4 million for Q4-2016
Partnerships	Rigosertib is partnered with SymBio Pharmaceuticals in Japan/Korea Onconova retains rights to the rest of the world
**As of 12-31-2016*	

ONCONOVA HIGHLIGHTS

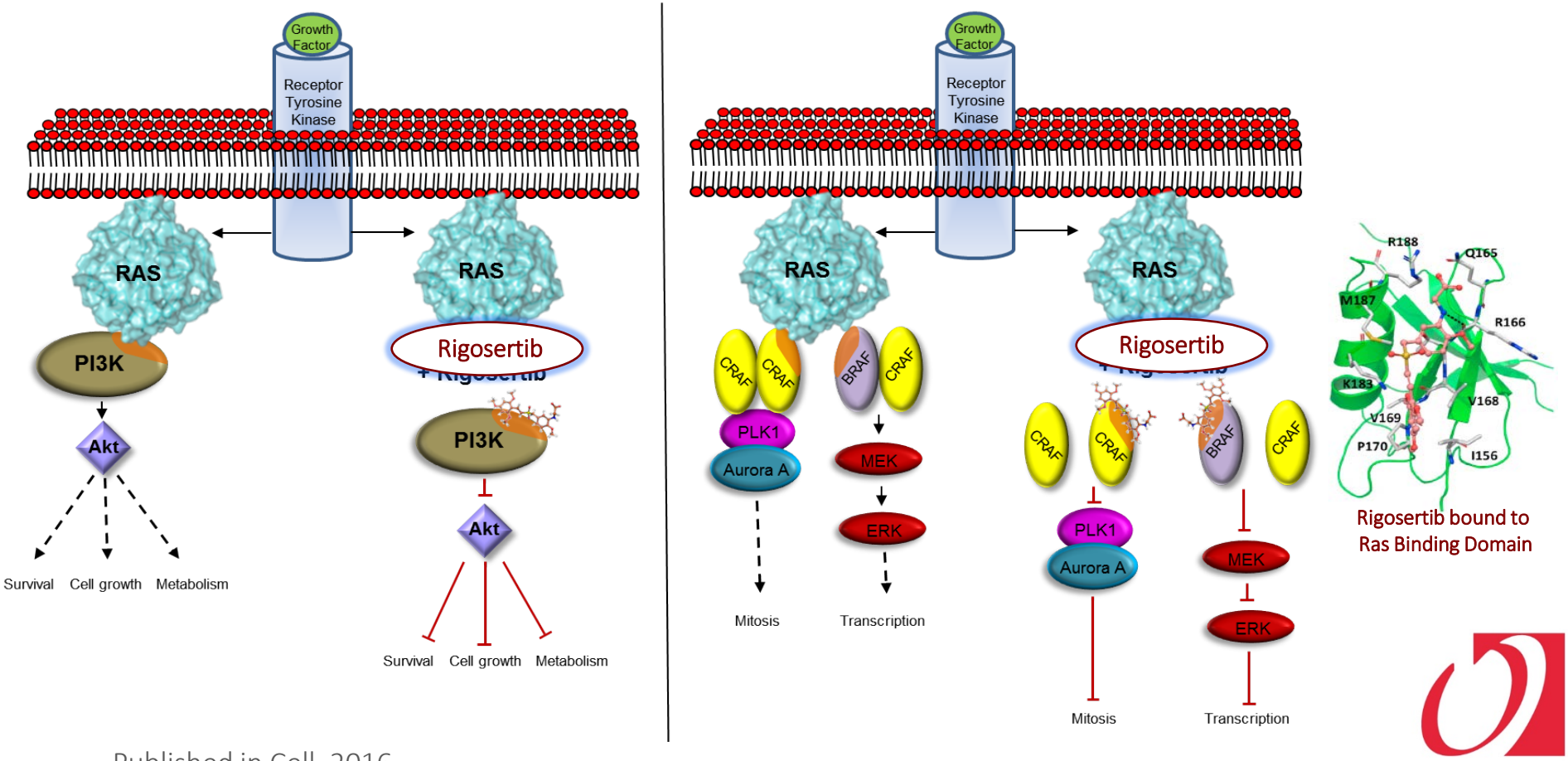
- Targeting underserved market in Myelodysplastic Syndromes (MDS)
  - >10,000 patients diagnosed annually in the U.S. with Higher-risk (HR) MDS
  - No new approved treatments in over 10 years
- Phase 3 Trial (INSPIRE) is underway on 4 continents for 2nd line HR-MDS
- Patents & orphan designation for MDS in the US, Europe and Japan
- Rigosertib partnered with SymBio in Japan/Korea
- Designing Ph. 3 trial for Oral rigosertib + azacitidine combination therapy
  - 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

ONCONOVA MDS PIPELINE



NOVEL MECHANISM OF ACTION

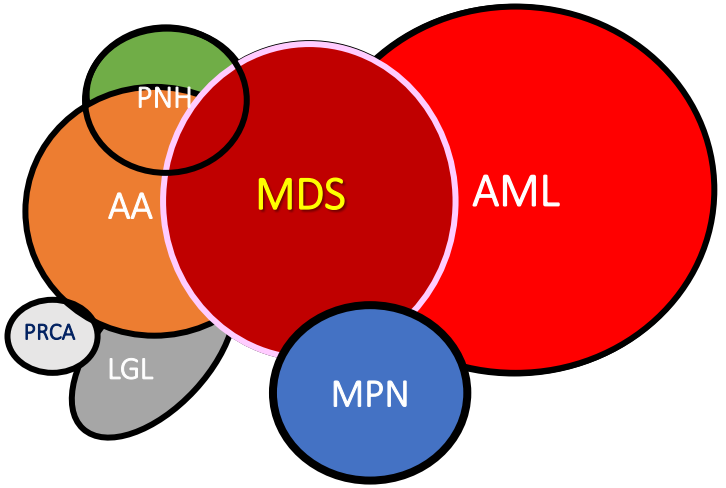
Rigosertib is believed to block downstream signaling by RAS effectors including PI3K and RAF by binding to Ras Binding Domain (RBD) found in many effector proteins



Published in Cell, 2016

MDS OVERLAPS WITH OTHER DISEASES

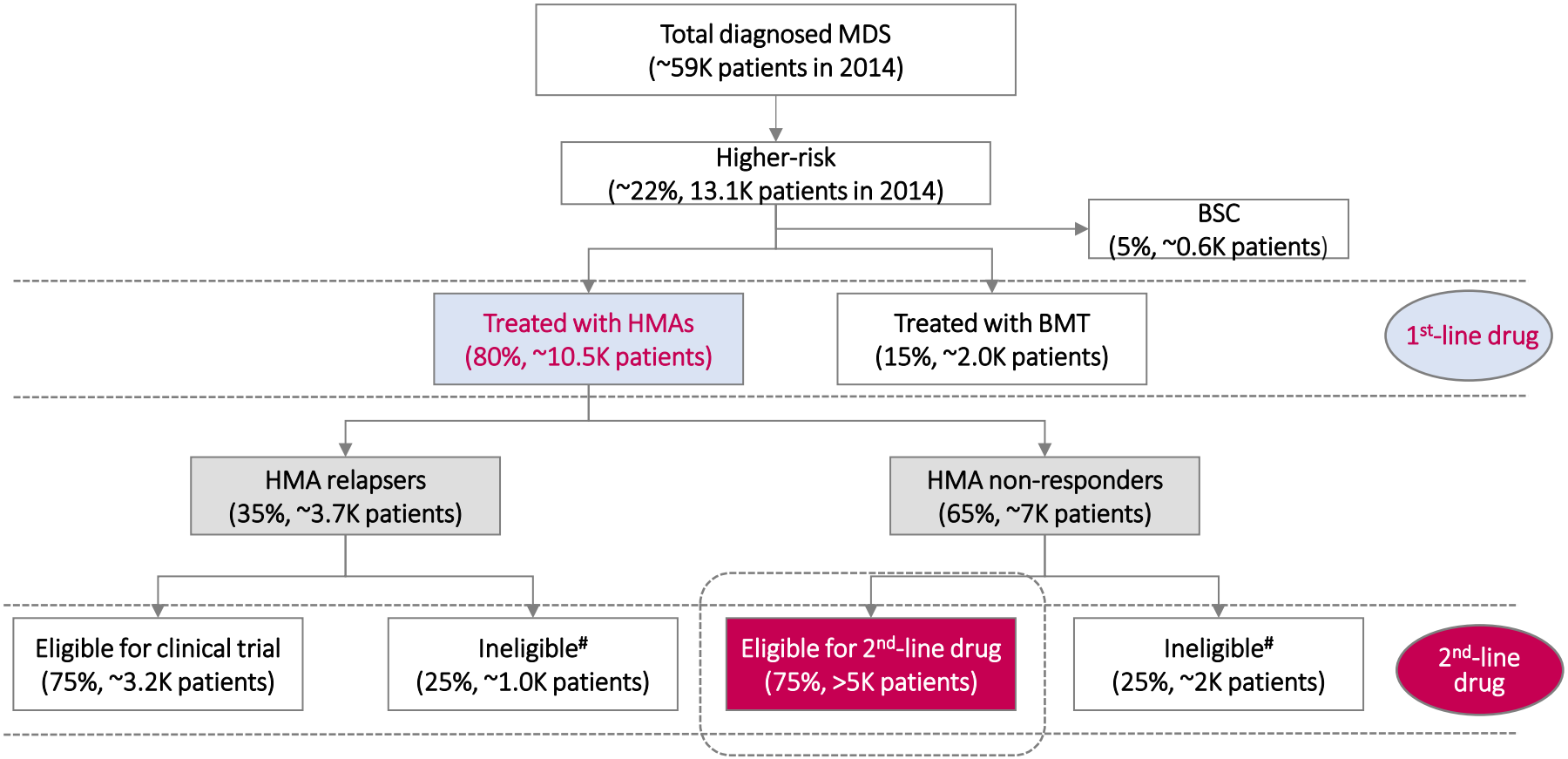
- MDS, a malignant hematopoietic stem cell disorder, is characterized by:[1]
  - Bone marrow failure
  - Cytopenias
  - 30% of patients progress to AML
- US prevalence estimate is 59,000
  - 18,000 have higher risk MDS
- Treatment options limited to hypomethylating agents (HMAs)
  - Vidaza (Celgene); Dacogen (Eisai/J&J)
  - Both approved a decade ago



Slide credit: clinicaloptions.com

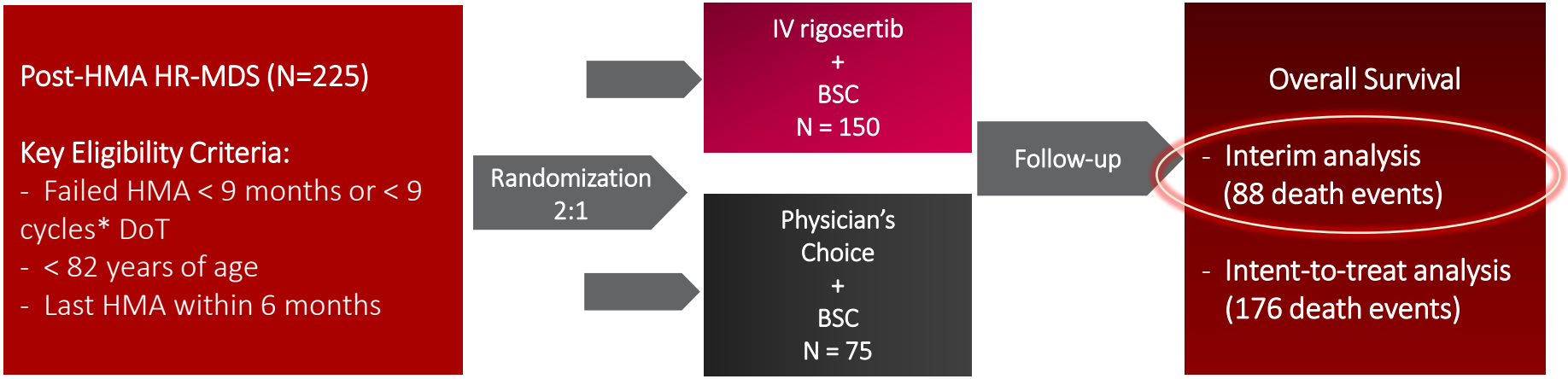
[1]Young NS. Ann Intern Med. 2002;136:534-546.

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



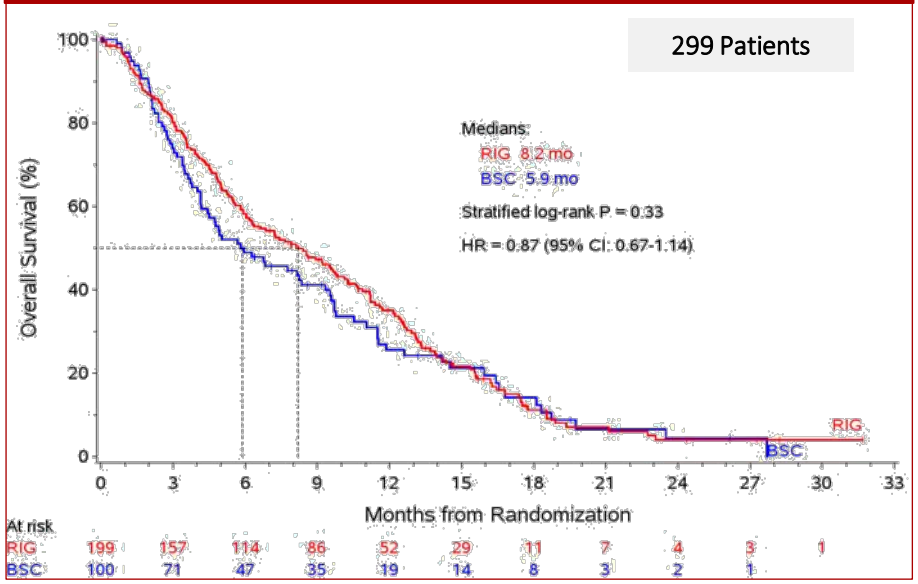
**9 cycles within 12 months of starting treatment*

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

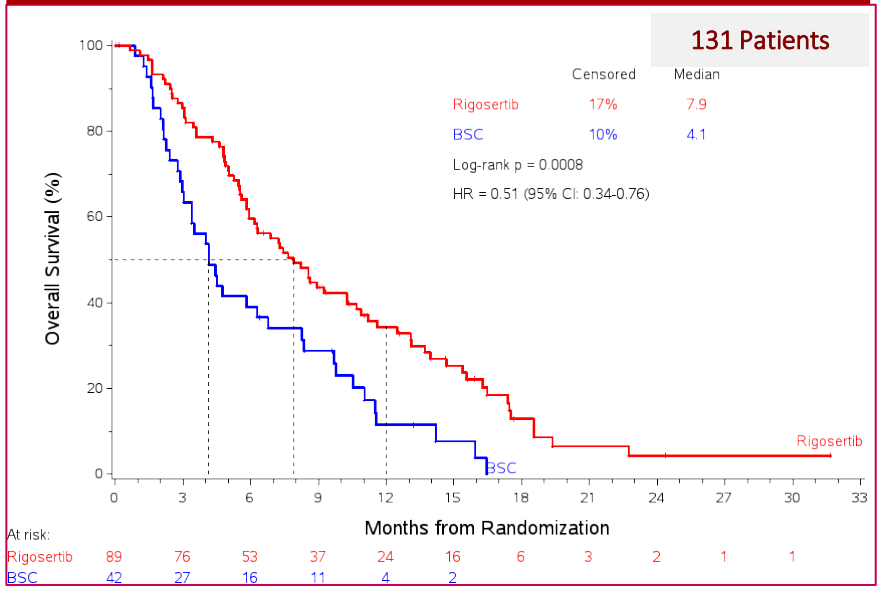
PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

Data from ONTIME paper* published in *Lancet Oncology*

ITT 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 = 0.51; P = 0.0008

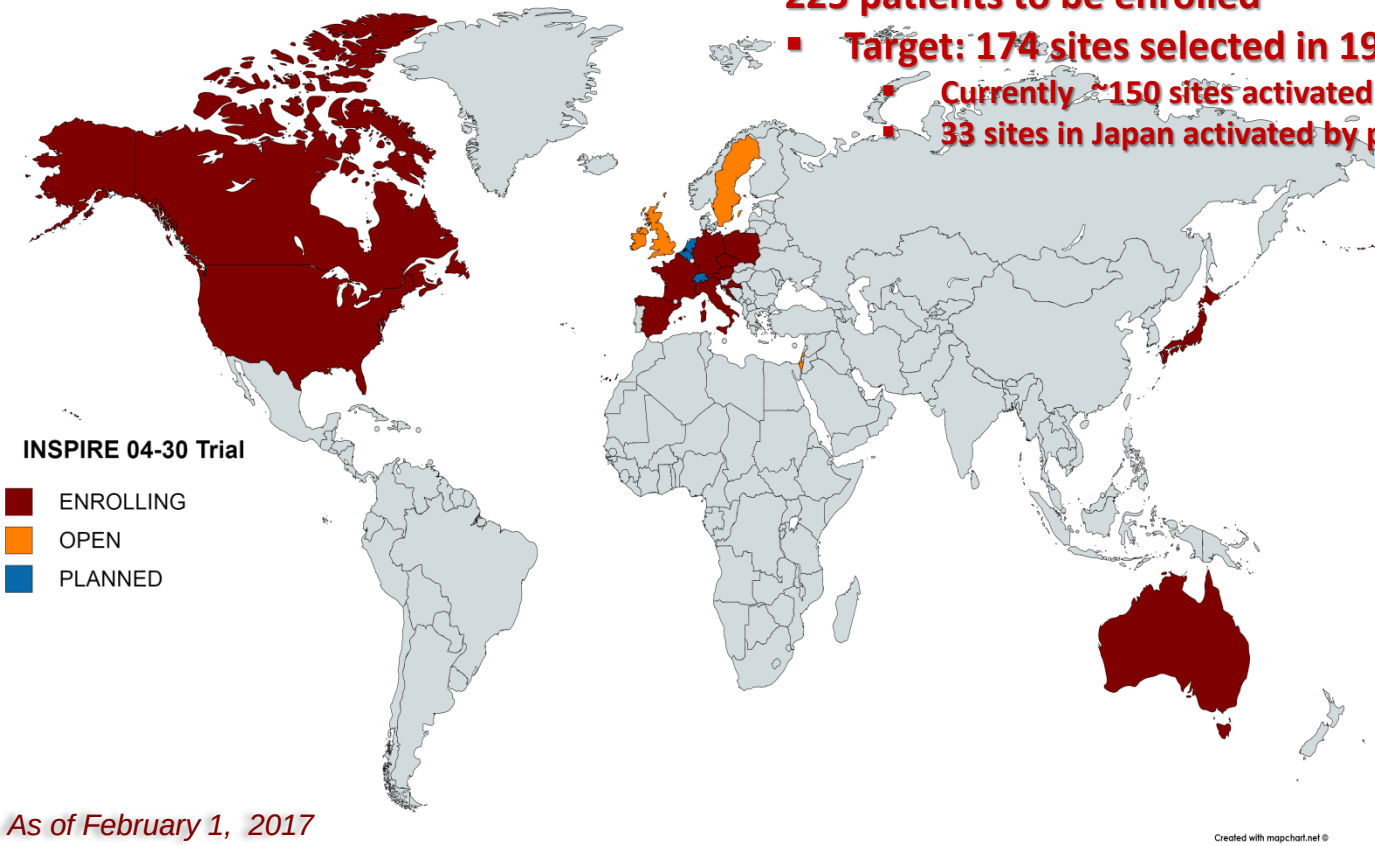
*Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, et al. Rigosertib versus best supportive care for patients with higher-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, Phase 3 trial; *The Lancet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

GLOBAL INSPIRE TRIAL PROGRESS

*The **IN**ternational **S**tudy of **P**hase III **I**V **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.*

225 patients to be enrolled

- **Target: 174 sites selected in 19 countries on 4 continents**
  - **Currently ~150 sites activated in 16 countries by Onconova**
  - **33 sites in Japan activated by partner SymBio**



As of February 1, 2017

Latest guidance (March 27 analyst 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

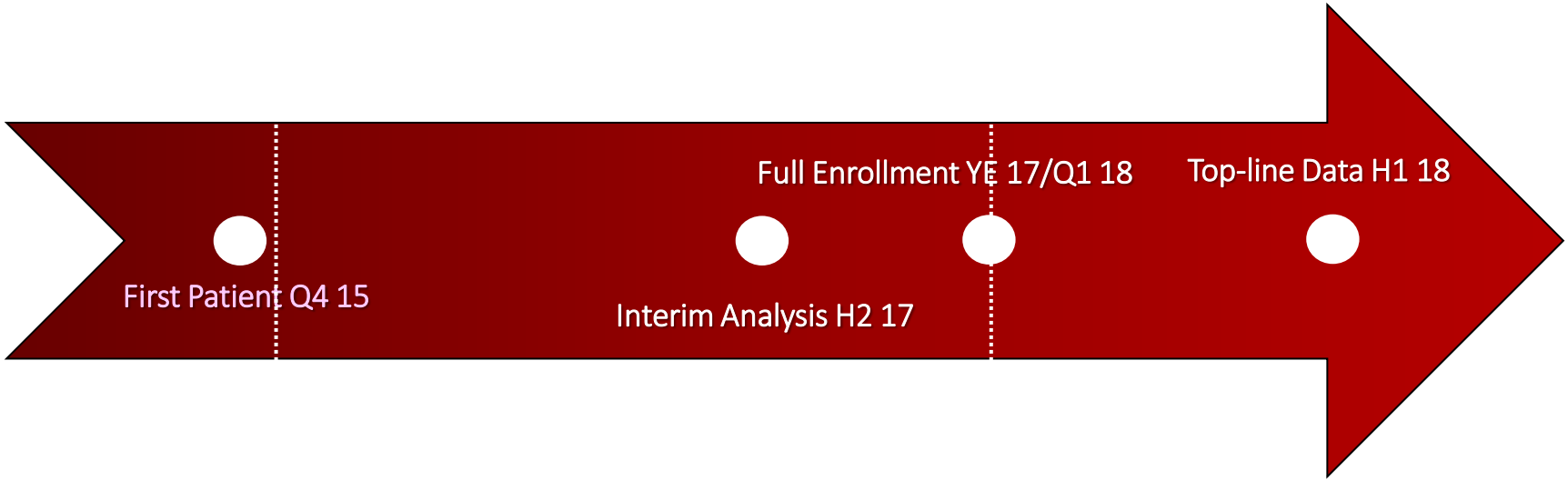
- **Maria R. Baer, MD - University of Maryland Greenebaum Cancer Center, Baltimore**
- Robert H. Collins, Jr., MD, FACP - **University of Texas Southwestern Medical Center, Dallas**
- **Guillermo Garcia-Manero, MD - University of Texas MD Anderson Cancer Center, Houston***
- **Lucy Godley, MD, PhD - 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

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

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

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

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

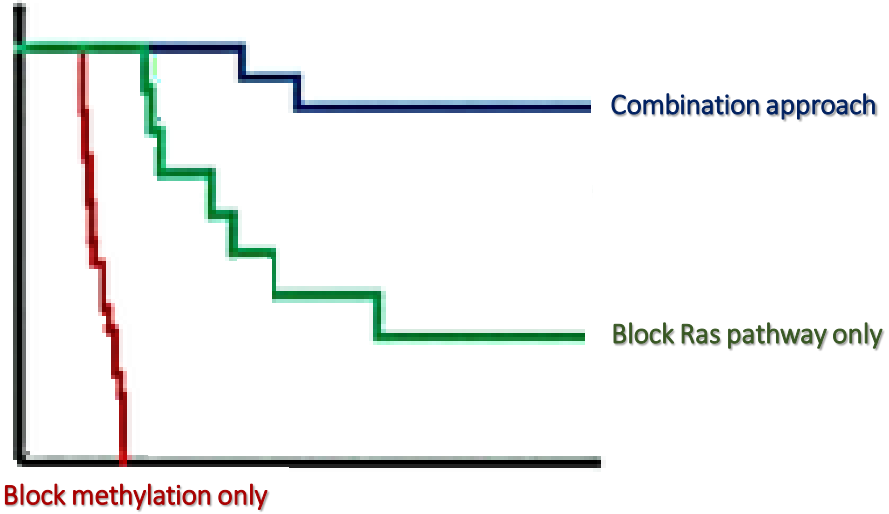
- Later stage mutations
- May be addressed by rigosertib

Combination approach

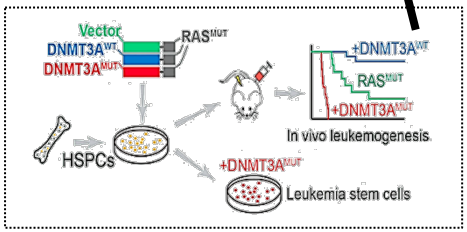
- Addresses more molecular defects
- Potential for synergistic activity

AML Animal Model

Validation of combination approach



Lu et al., 2016 *Cancer Cell*



COMBINATION THERAPY PHASE 1/2 TRIALS

Combination oral Rigosertib + Azacitidine in MDS patients

Included a diverse patient population including

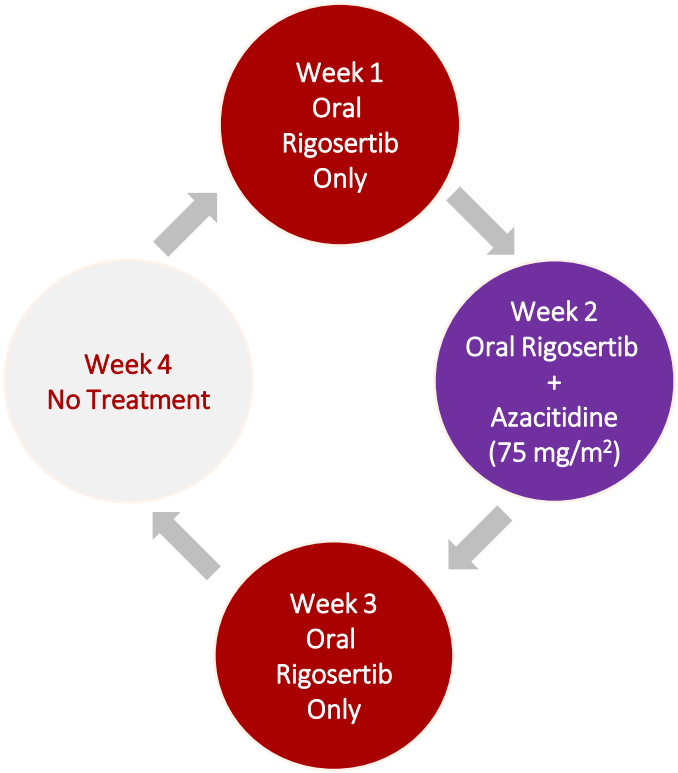
- HMA-naïve front-line patients
- HMA pre-treated second-line patients
- AML patients

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

NEXT STEPS FOR RIGOSERTIB + AZACITIDINE DEVELOPMENT

Key Parameters and Milestones for Oral Rigosertib + Azacitidine Phase 3 Program		
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

RIGOSERTIB IS PARTNERED IN JAPAN/KOREA
SINCE 2011

Partnerships sought in other territories

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*

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

ONCONOVA
TARGETING CANCER | PROTECTING HEALTHY CELLS

ir@onconova.us

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

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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

REVISED IPSS: PROGNOSTIC SCORE VALUES AND RISK CATEGORIES/SCORES

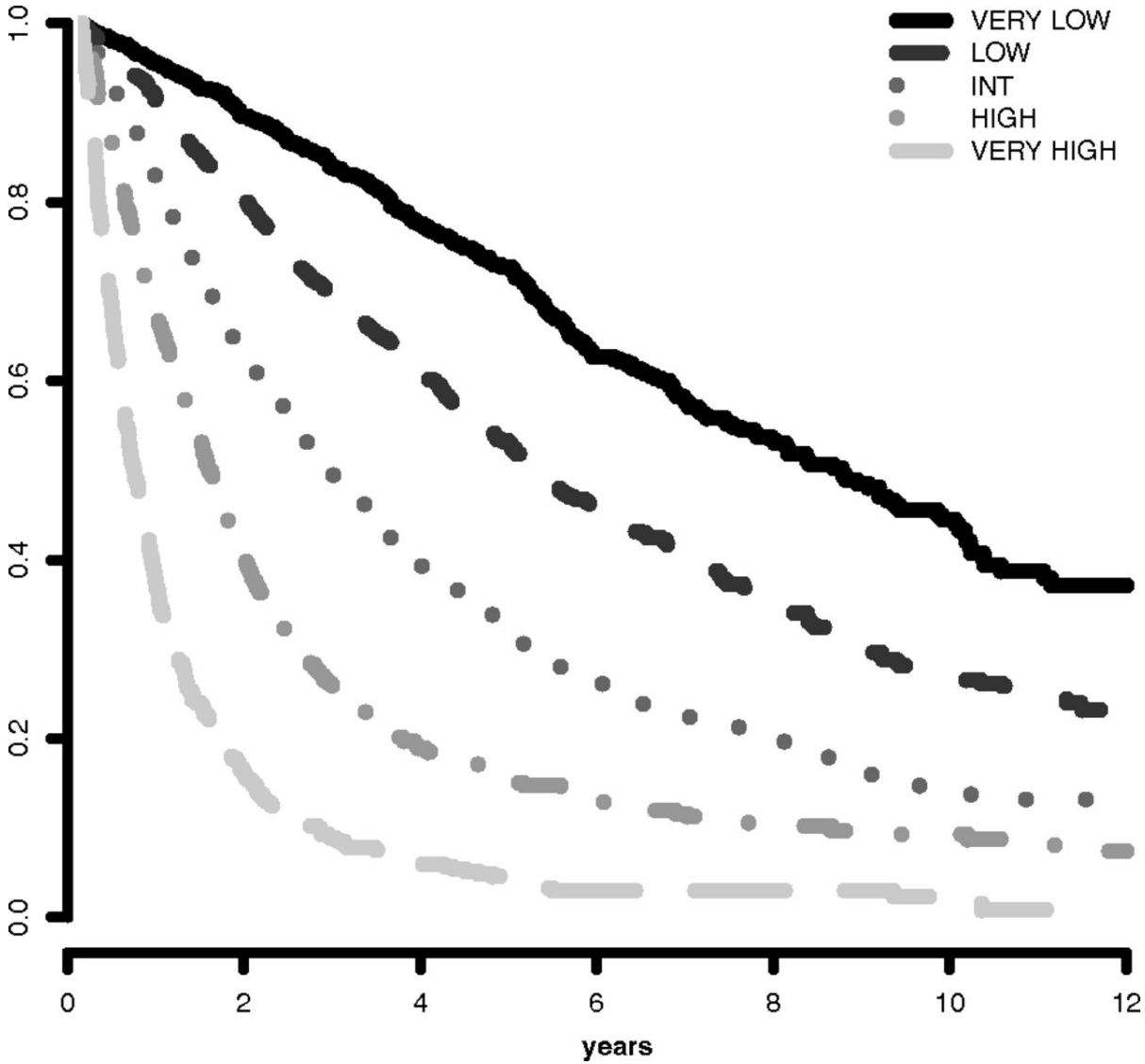
Prognostic Variable	Prognostic Score Value						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good	--	Good	--	Intermediate	Poor	Very poor
BM blast, %	≤ 2	--	> 2 to < 5	--	5-10	> 10	--
Hemoglobin, g/dL	≥ 10	--	8 to < 10	< 8	--	--	--
Platelets, x 10^9/L	≥ 100	50 to < 100	< 50	--	--	--	--
ANC, x 10^9/L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



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