ONCONOVA THERAPEUTICS

TARGETING CANCER, PROTECTING HEALTHY CELLS

Onconova Business Development Opportunities

5th Annual Cancer Biopartnering and Investor Forum

March 28, 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.

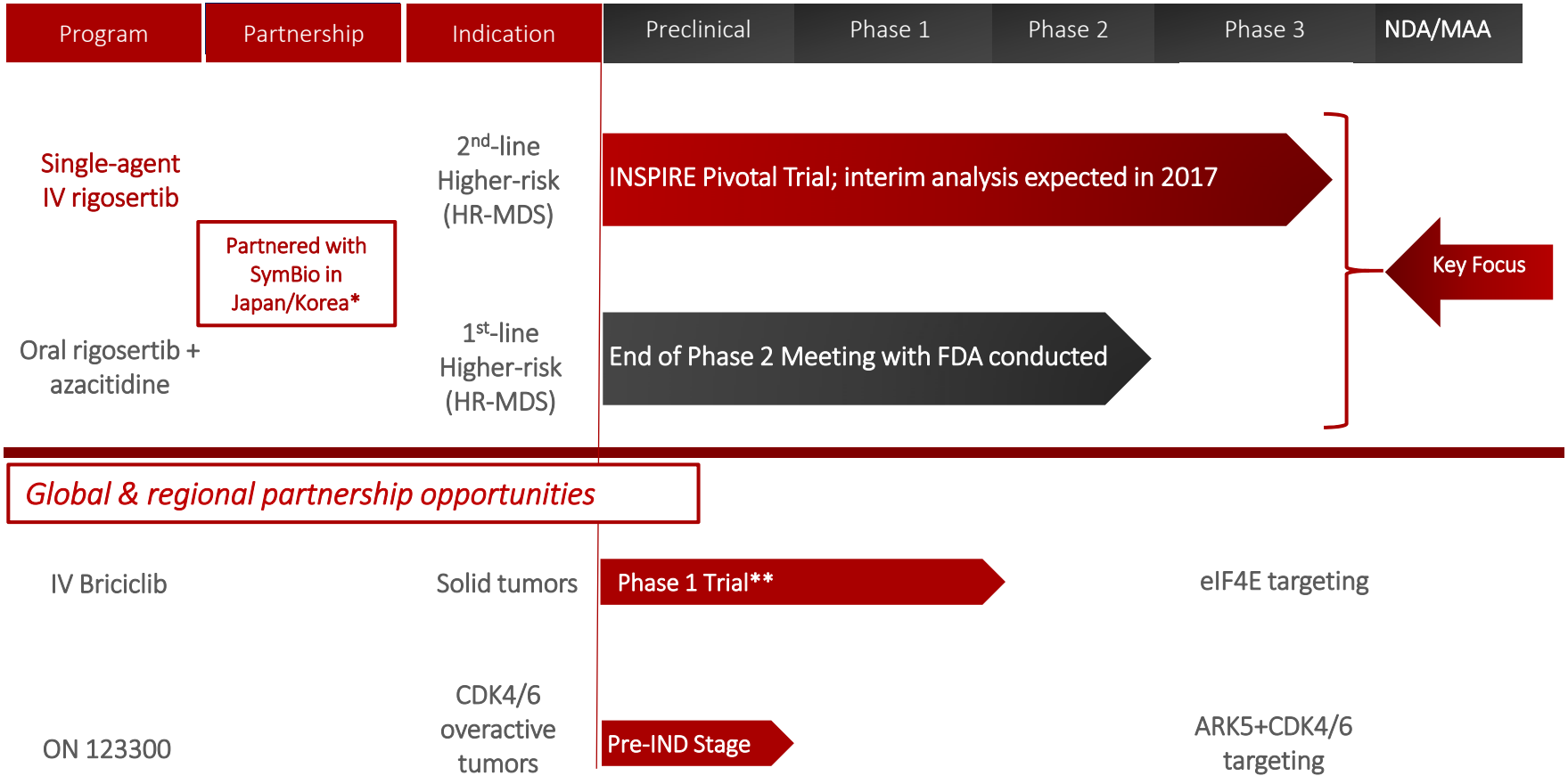
FINANCIAL DETAILS

Onconova founded in 1998; public since 2013	
Ticker	Nasdaq ONTX
Stock information	▪ 6.76 million shares* ▪ Public float 79% ▪ 52 week range $2.11-8.17 ▪ Average daily volume 85,000
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 $21.4 million*
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 per YE 2016 financials*	

ONCONOVA 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
- Issued 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, 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
- Pipeline assets beyond rigosertib for partnerships

ONCONOVA CANCER PRODUCT PIPELINE

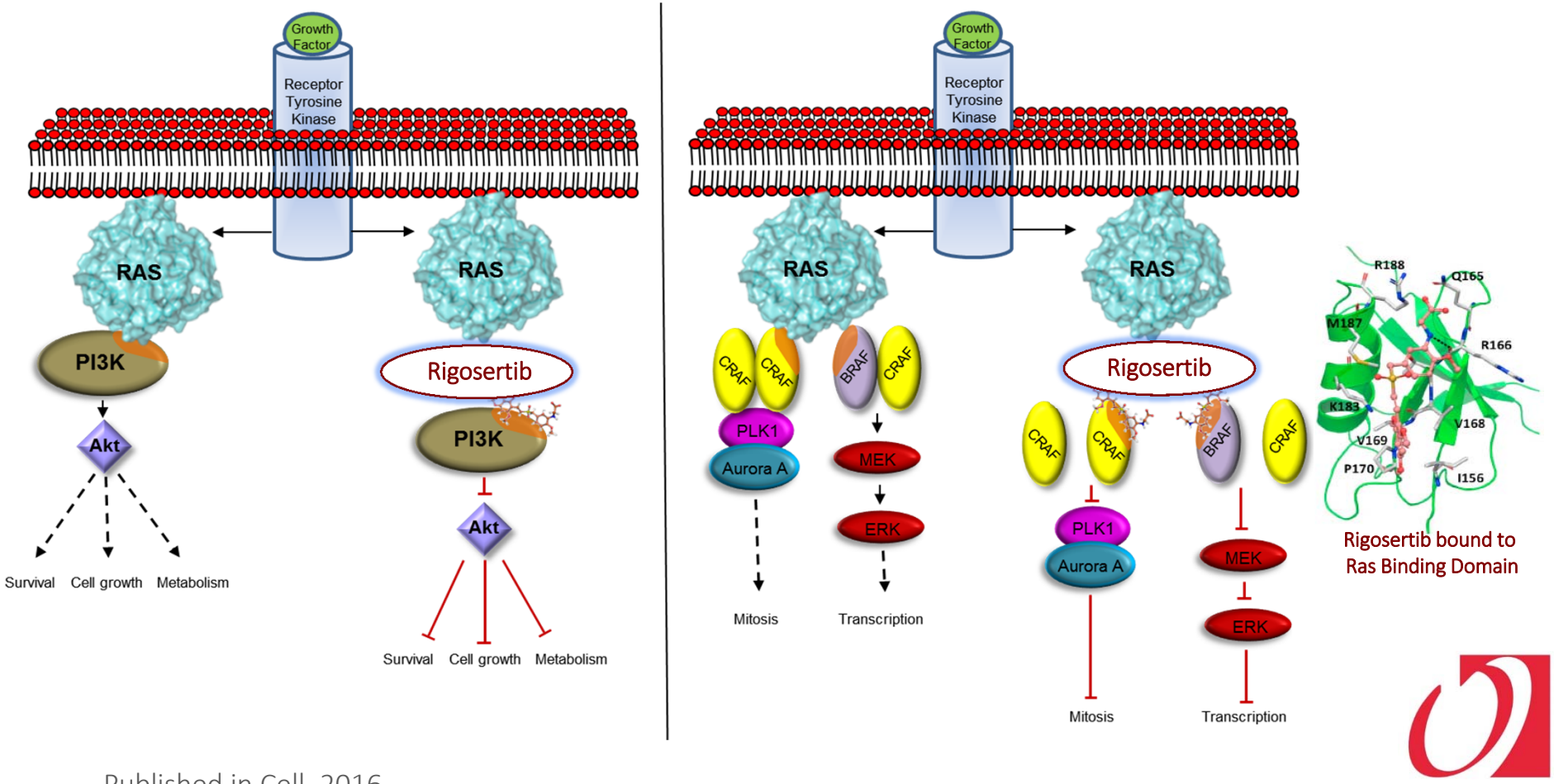


*Onconova retains rights elsewhere, including USA

**Trial on hold pending partnering and manufacturing of new clinical trial material (CTM)

NOVEL MECHANISM OF ACTION

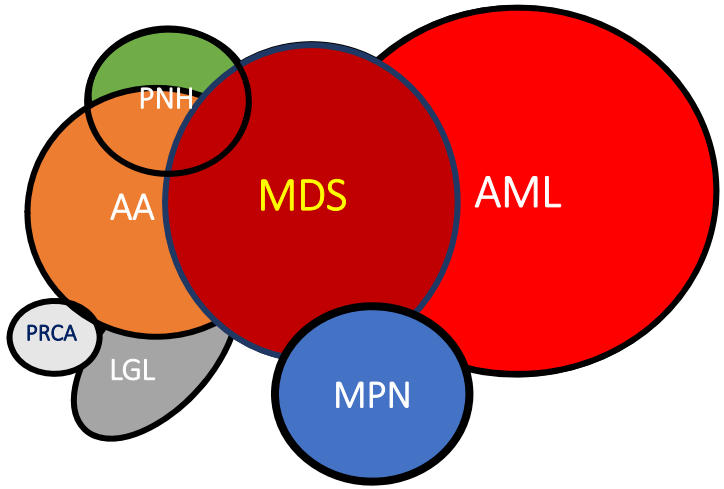
Rigosertib blocks downstream signaling by RAS effectors including PI3K and RAF by binding to Ras Binding Domain (RBD) found in many effector proteins



Published in Cell, 2016

MDS OVERLAPS WITH OTHER DISEASES

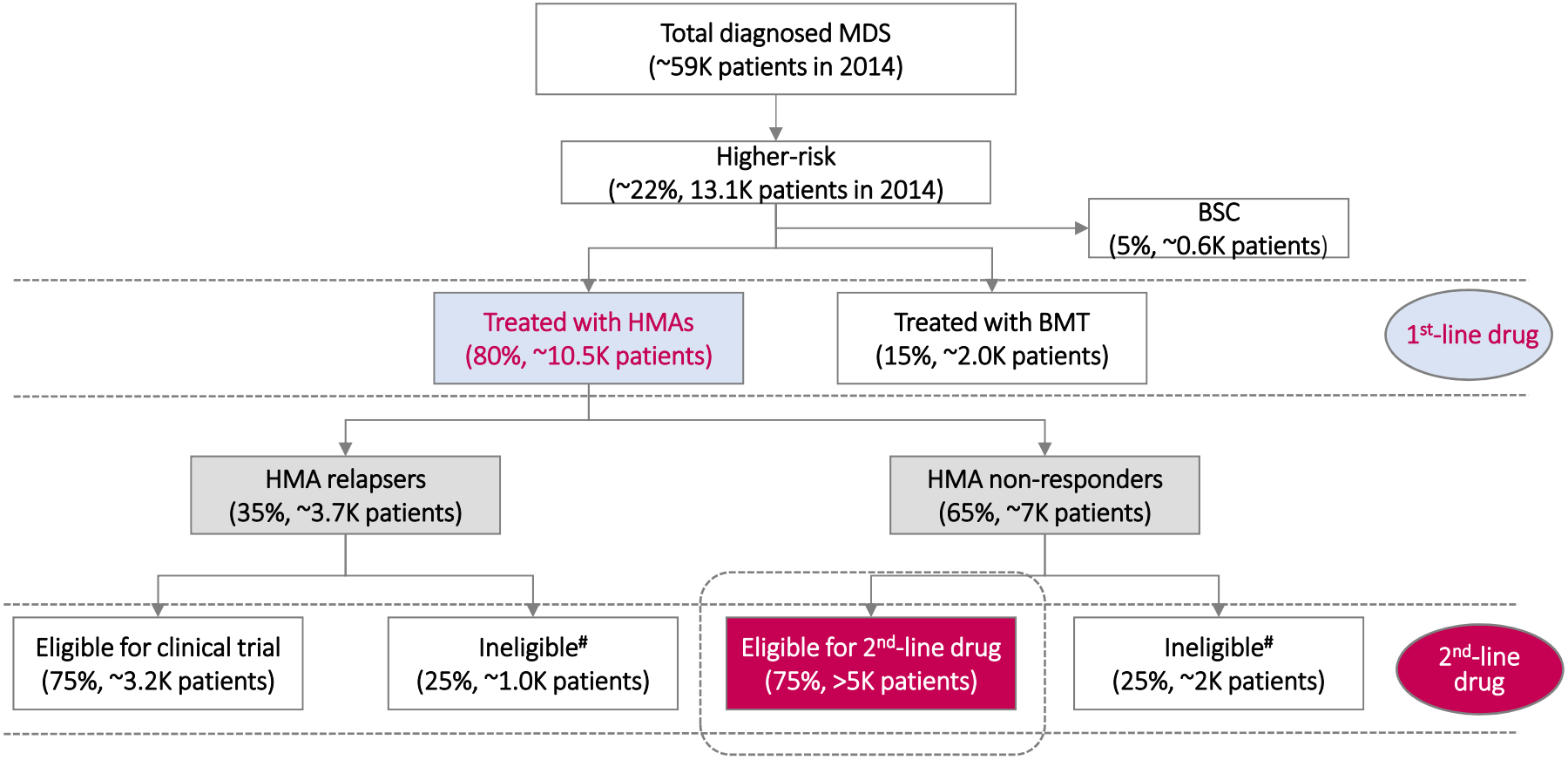
- MDS, a malignant hematopoietic stem cell disorder is characterized by:[1]
  - Bone marrow failure
  - Cytopenias
  - 30% of patients to progress to AML
- MDS has overlap with other hematological disorders
- A spectrum of risk, from low to very high, measured by IPSS-R scores.
- US prevalence estimate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



Slide credit: clinicaloptions.com

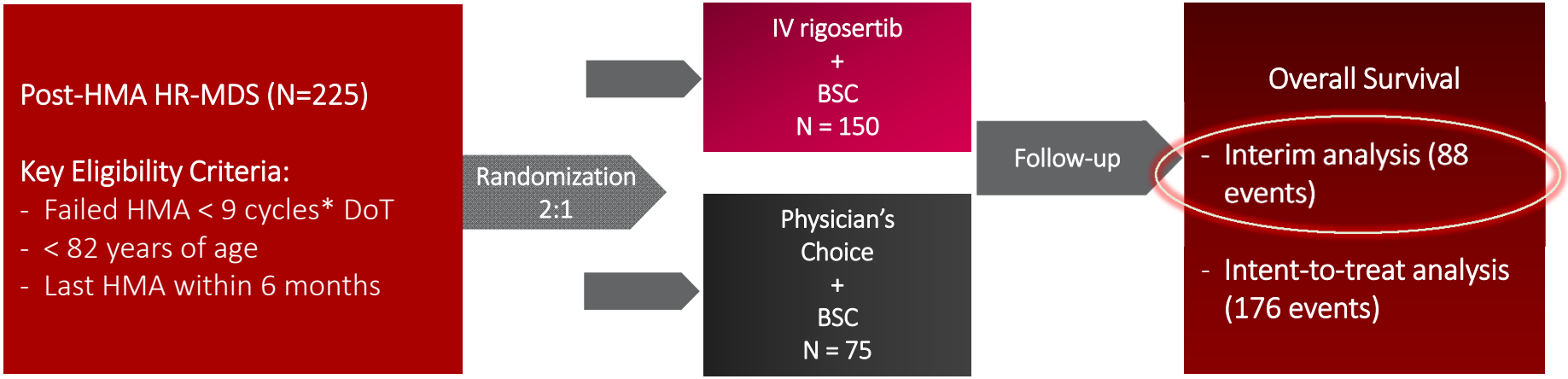
[1]Young NS. Ann Intern Med. 2002;136:534-546.

RIGOSERTIB IN HIGHER-RISK MDS



- Rigosertib is being developed for 2nd-line patients (INSPIRE Phase 3 trial)
  - 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



**9 cycles within 12 months of starting treatment*

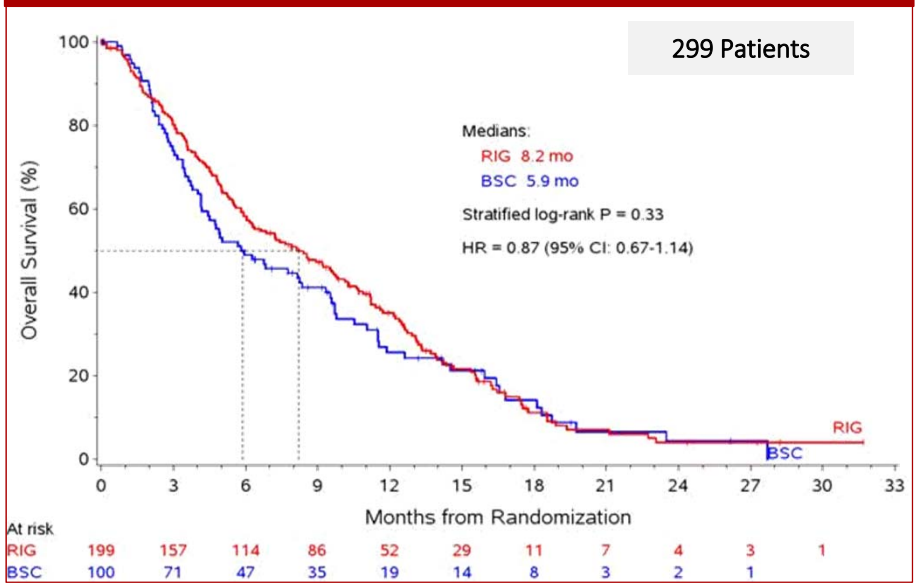
- Statistical analysis: two analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Trial can succeed in two ways: ITT population or IPSS-R Very High Risk
- Genomic sequencing of patient samples

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

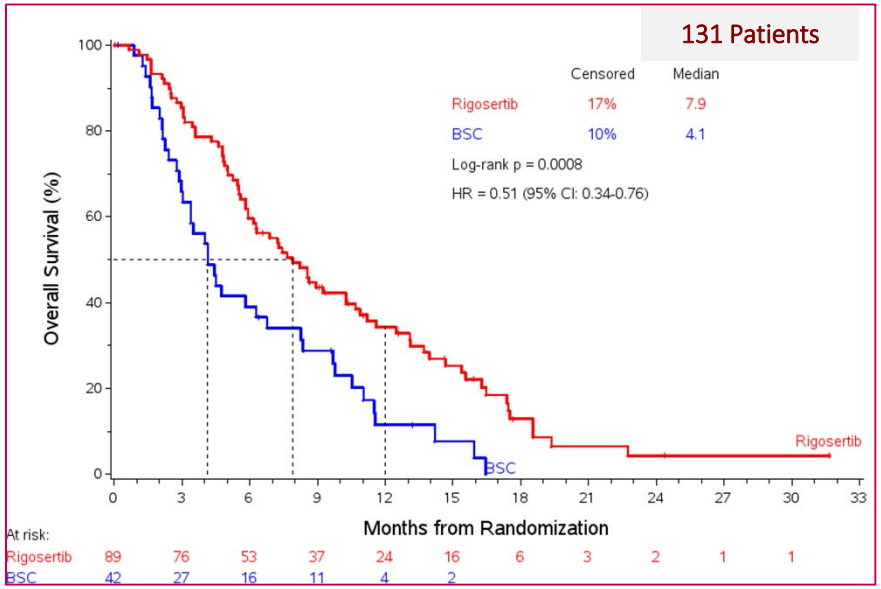
PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

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 = 0.51; P = 0.0008

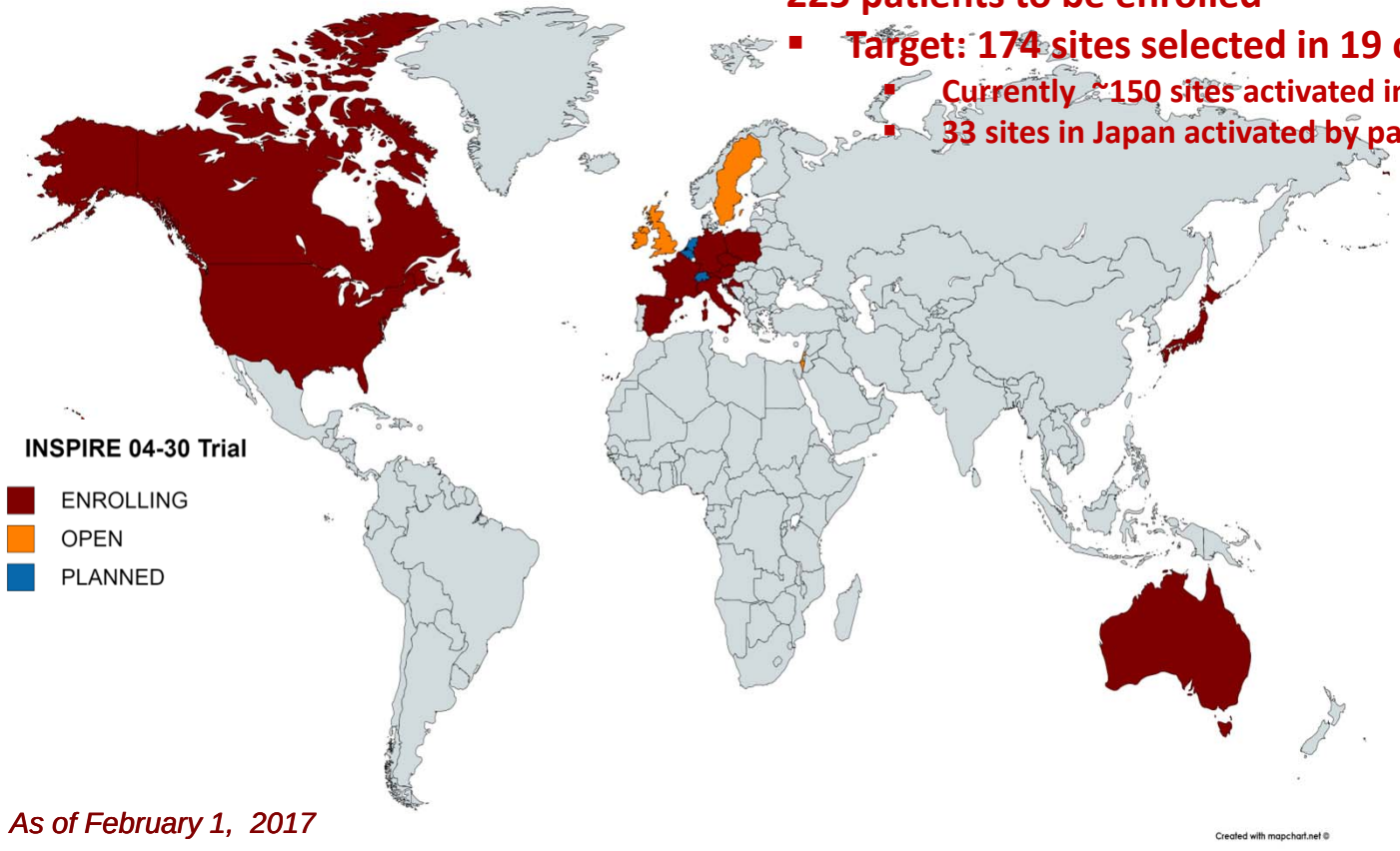
*Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, et al. Rigosertib versus best supportive care for patients with higher-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, Phase 3 trial; *The Lancet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

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 Pivotal Trial

ONTIME participants in red (highest accruing sites in bold)

Sites in Japan not included in this list

Sites in USA

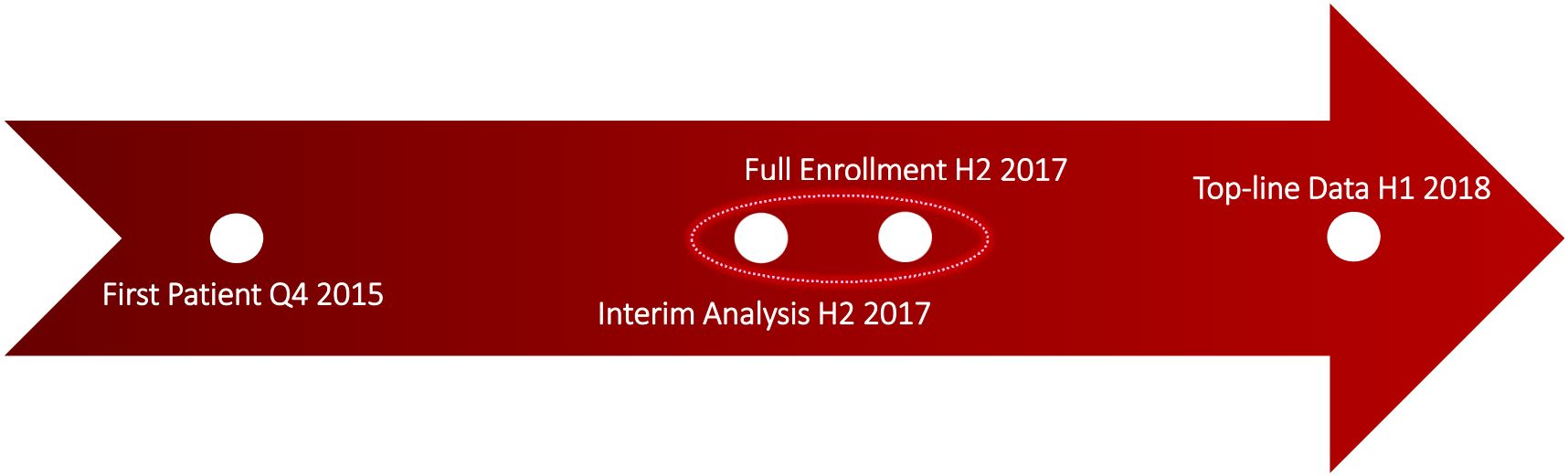
- Maria R. Baer, MD - University of Maryland Greenebaum Cancer Center, Baltimore
- Robert H. Collins, Jr., MD, FACP - University of Texas Southwestern Medical Center, Dallas
- Guillermo Garcia-Manero, MD - University of Texas MD Anderson Cancer Center, Houston*
- Lucy Godley, MD, PhD - University of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

DATA ANALYSIS FOR INSPIRE TRIAL



- Key features of INSPIRE trial
  - Targeted population of post-HMA patients
  - Running in North America, Europe, Israel, Australia and Japan
  - Primary endpoint is overall survival
    - Entire trial (ITT analysis) after 176 events have occurred
    - If the ITT analysis is negative, a 2nd analysis of IPSS-R VHR subgroup is permitted

- Interim analysis planned
  - ITT analysis after 88 events

EPIGENETIC AND GROWTH FACTOR PATHWAY MUTATIONS SYNERGIZE IN INDUCING LEUKEMIC TRANSFORMATION

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

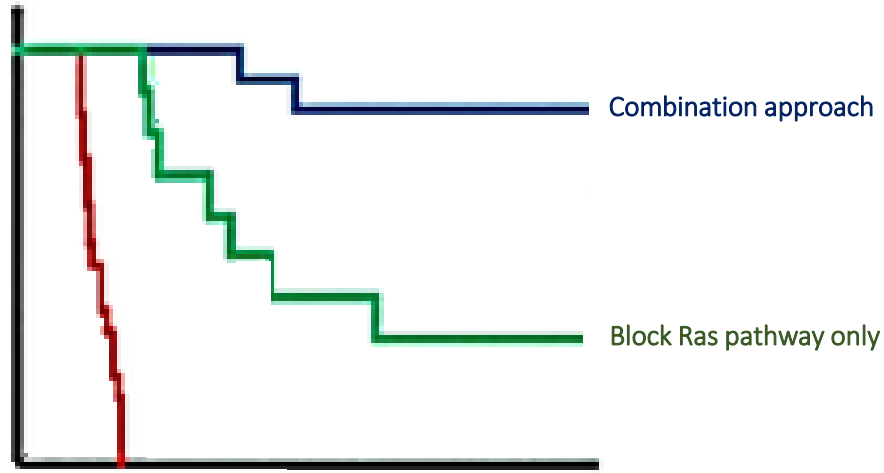
- Later stage mutations
- May be addressed by rigosertib

Combination approach

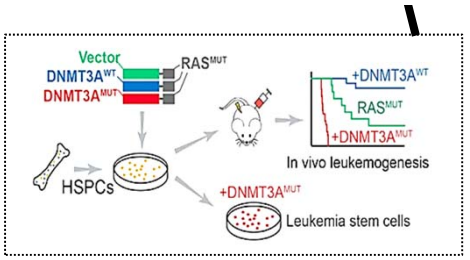
- Addresses more molecular defects
- Potential for synergistic activity

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

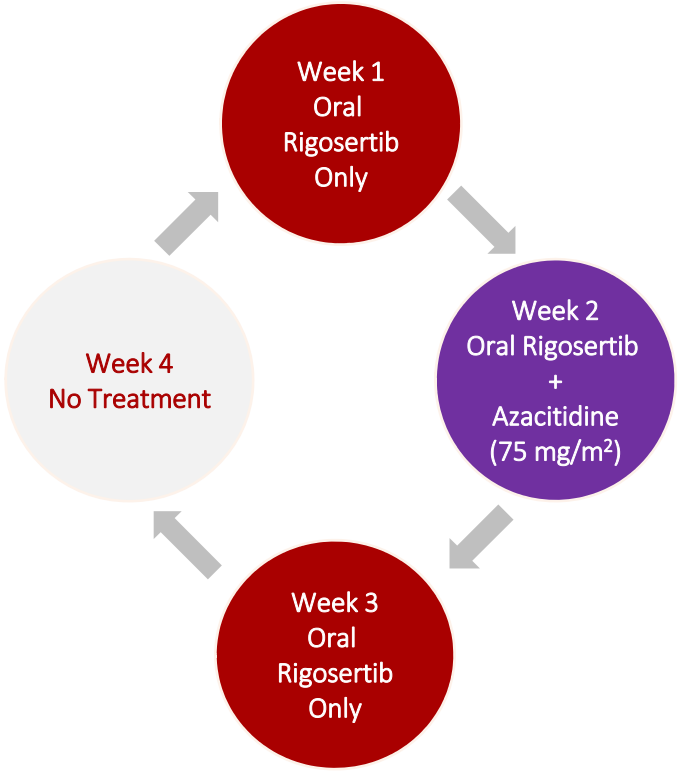
- HMA-naïve front-line patients
- HMA pre-treated second-line patients
- AML patients

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%)

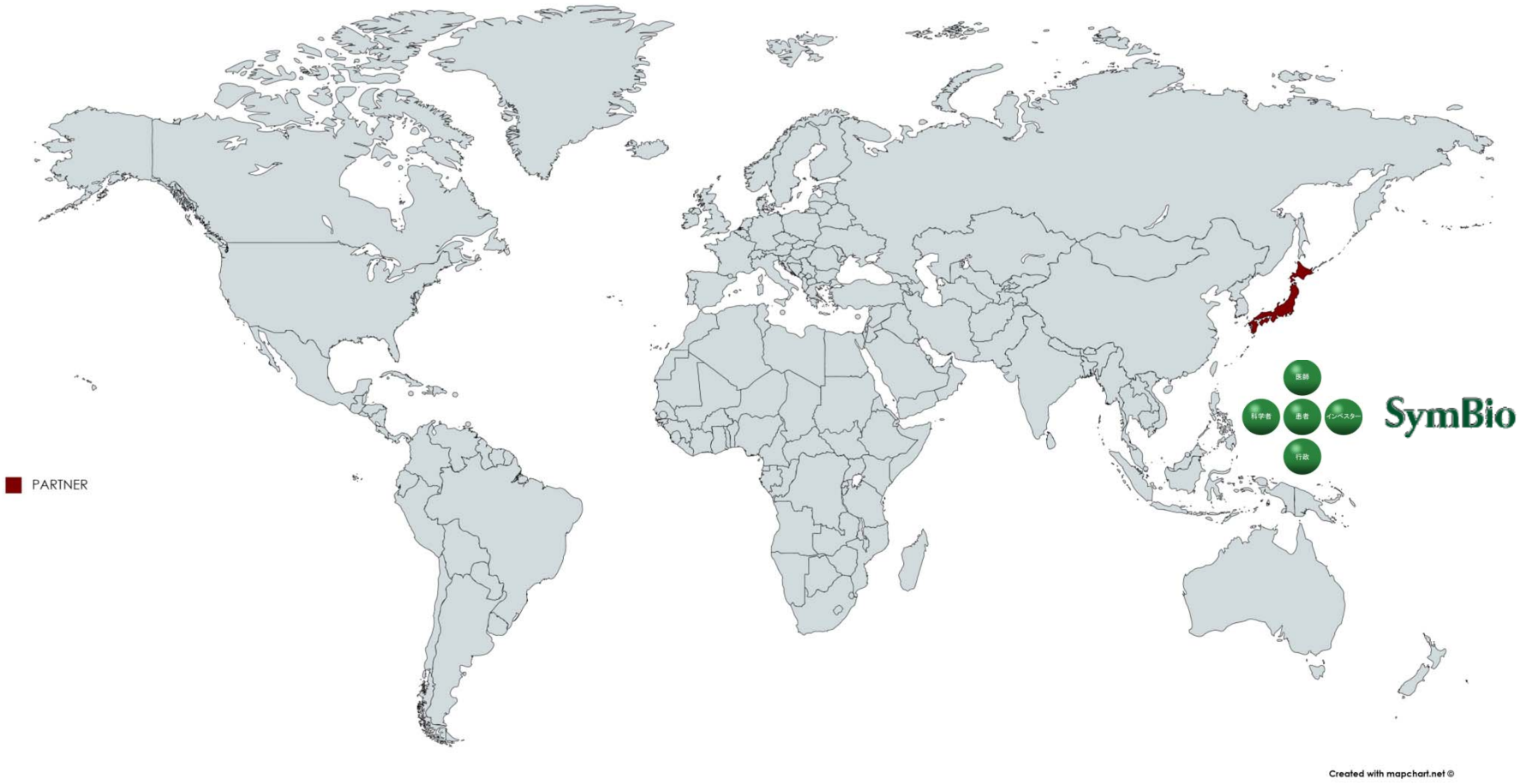
*All responders had CR and no PR was noted in this study

**Several published studies show 6-20% CR with single agent azacitidine and overall response of 40-45%

NEXT STEPS FOR RIGOSERTIB + AZACITIDINE DEVELOPMENT

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

RIGOSERTIB IS PARTNERED IN JAPAN/KOREA
SINCE 2011



Partnerships sought in other territories

ONCONOVA PRODUCT CANDIDATE PIPELINE

Not including Rigosertib

Partnerships sought for earlier stage 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**	**Preclinical**	**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 α/δ**	**Pre-clinical**	**Toxicology**	**IPI-145**	**In process**

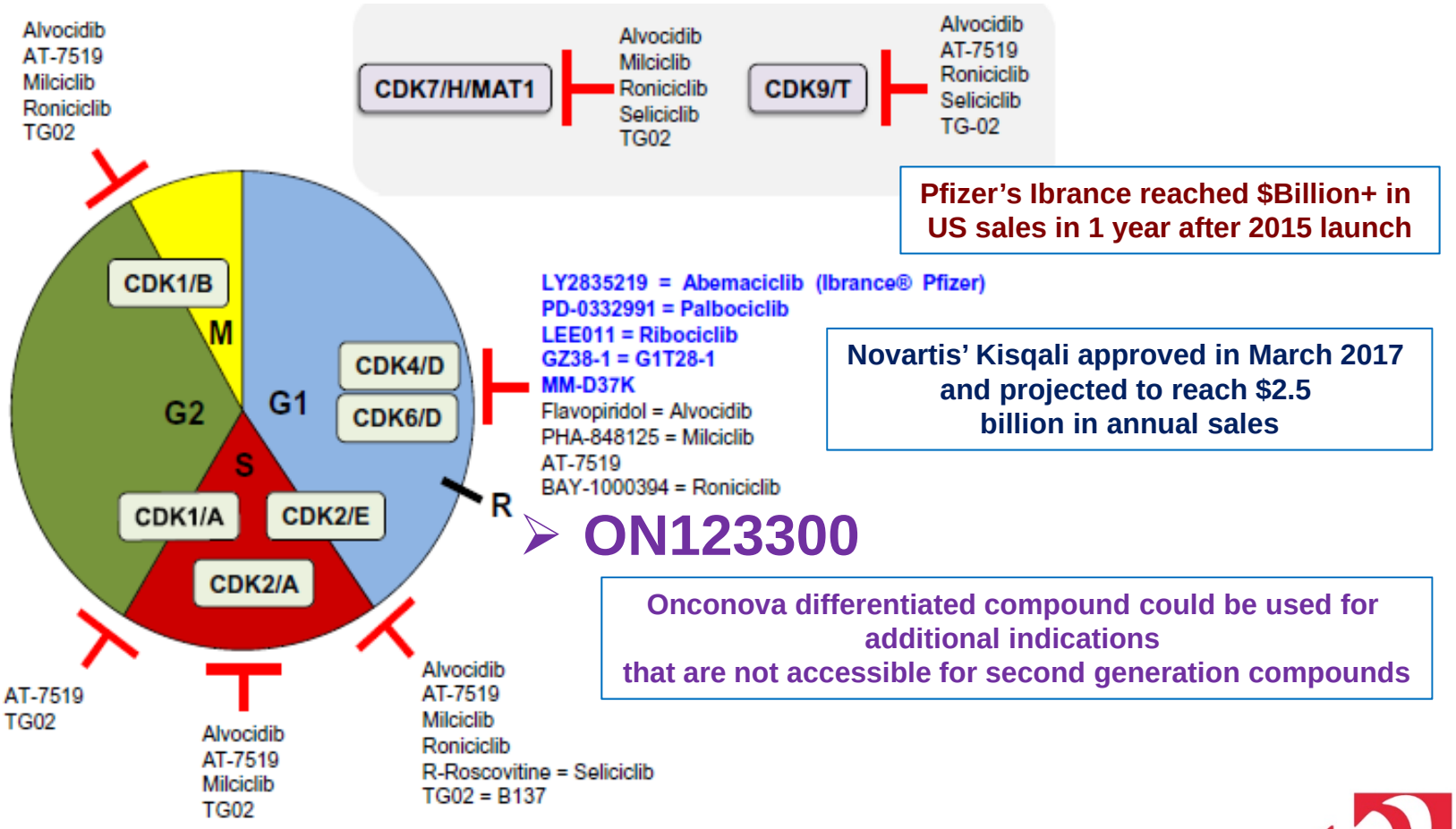
Patent protected, differentiated small molecule compounds

ON 123300: A DIFFERENTIATED THIRD-GENERATION CDK4/6 INHIBITOR

- Recently launched IBRANCE® (Palbociclib, Pfizer) has been considered a success story
  - ~10 month increase in PFS, approved in combination with letrozole
  - ~$2BN annual sales (2016)

- **ON 123300** has several **differentiating features**
  - In addition to CDK4/6 also targets emerging ARK5 controlling cellular metabolism and survival
  - Potential to act as single agent – induces apoptosis and hence is both cytotoxic and cytostatic
  - Potential to affect emergence of resistance (RB negative setting)
  - Differentiated pre-clinical activity
    - breast cancer,
    - mantle cell lymphoma,
    - multiple myeloma and
    - colorectal cancer cell lines, primary patient samples and xenografts
  - Potentially reduced effect on neutropenia
  - Effect on cell migration
  - BBB penetrating properties
  - Suitable for indications that may not be amenable to palbociclib like compounds

NEW GENERATION OF CDK4/6 INHIBITORS ARE VALIDATED DRUGS



Pfizer's Ibrance reached $Billion+ in US sales in 1 year after 2015 launch

Novartis' Kisqali approved in March 2017 and projected to reach $2.5 billion in annual sales

Onconova differentiated compound could be used for additional indications that are not accessible for second generation compounds

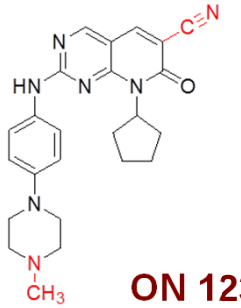
Figure 5. Cell cycle and transcription regulation CDK inhibitors under clinical evaluation. Specific CDK4 and CDK6 inhibitors are indicated in blue.

* C. Sánchez-Martínez et al./Bioorg. Med. Chem. Lett. 25 (2015) 3420–3435

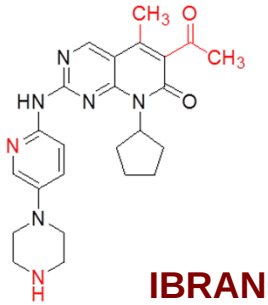
ON 123300: DIFFERENTIATED TARGET SPECIFICITY

Kinase	Comparative IC_{50} profile (nM)	
	ON 123300	IBRANCE®
ARK5	4.95	>5000
CDK4/D1	3.87	5.36
CDK6/D1	9.82	3.76

Comparison of Two Compounds in Reaction Biology Kinase Assays



ON 123300

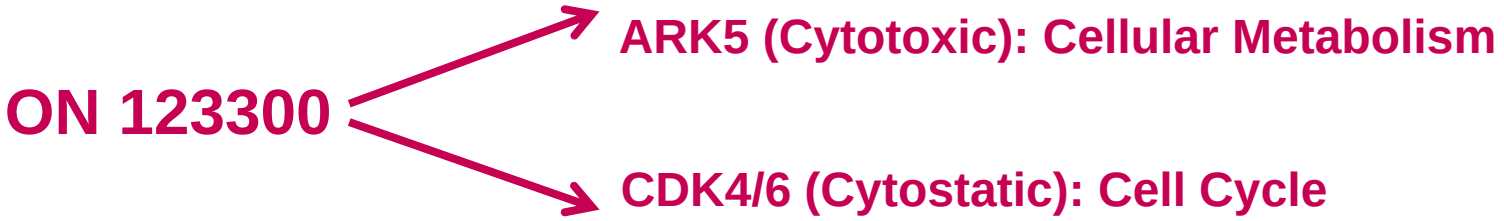


IBRANCE®

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

ON 123300: A DIFFERENTIATED THIRD-GENERATION CDK4/6 INHIBITOR

ADDITIVE/ SYNERGISTIC EFFECT from Targeting both Cell Cycle and Metabolism Pathways



- Dual inhibition results in the following benefits:
  - Activity in Rb negative setting
  - Apoptosis
  - Single agent activity
  - Other differentiating features including autophagy, cell migration, reduced neutropenia

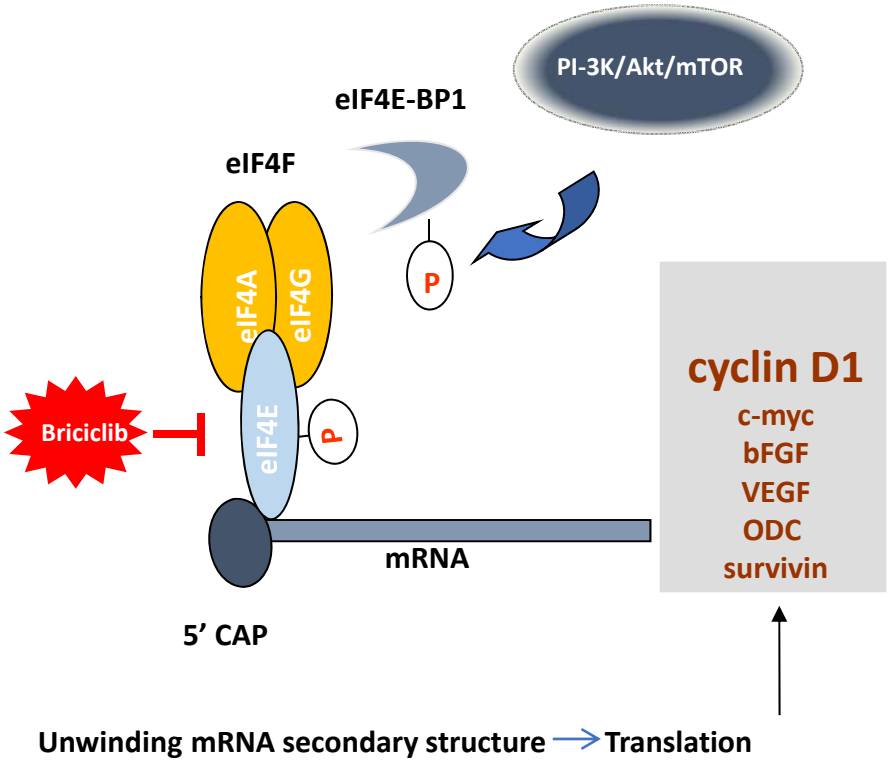
Animal models (xenografts) for breast, colon, myeloma and Mantle Cell Lymphoma available

BRICICLIB: PHASE 1 STAGE INHIBITOR OF EIF4E

- Phase 1 stage targeted anticancer agent
  - Strong IP protection spanning to at least 2025
  - **Novel target relevant to refractory cancers**
    - Binds to eIF4E to inhibit translation of oncoproteins like cyclin D1
- Development status
  - Open IND
  - Phase 1 all-comers trial 08-02 opened in July 2014; six cohorts completed with no DLTs identified
- Broad indication potential
  - Certain solid tumors
  - MCL and other lymphomas
  - Single agent and combination therapy

EIF4E IS A CRITICAL REGULATORY HUB

- eIF4E is high-profile nodal protein target
- eIF4E is required to allow PI3K, AKT and MTOR to act as oncogenes
- Antisense and indirect inhibition (MTORi/AKTi/PI3Ki) have been employed to target eIF4E
- Small molecule approaches and direct targeting have remained challenging
- **Briciclib is one of a few compounds known to directly bind to and inhibit eIF4E**



BRICICLIB PHASE 1 08-02 TRIAL DESIGN

- Entry criteria:
  - Patients with advanced cancer and solid tumors
- Drug administration:
  - IV 2-hour infusion weekly for 3 out of 4 week cycle
- Sites:
  - University of Colorado
  - Roswell Park
  - Sarah Cannon
- Endpoints:
  - Safety summary
  - Pharmacokinetics
  - Efficacy by RECIST
  - Cyclin D1 in responding patients

	Dose
Cohort 1	17 mg weekly
Cohort 2	35 mg weekly
Cohort 3	70 mg weekly
Cohort 4	140 mg weekly
Cohort 5	280 mg weekly
Cohort 6	560 mg weekly
Cohort 7	1120 mg weekly

- Final dosing cohort (1120 mg) will allow
  - Robust evaluation of safety from >30 patients
  - Efficacy and pharmacokinetics required for design of next clinical study
  - Opportunity to correlate efficacy with effect on eIF4E-related biomarker, cyclin D1
  - Recommended Phase 2 dose and Schedule

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

ONCONOVA
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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


ONCONOVA
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TARGETING CANCER, PROTECTING HEALTHY CELLS
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BACK-UP SLIDES

REVISED IPSS: PROGNOSTIC SCORE VALUES AND RISK CATEGORIES/SCORES

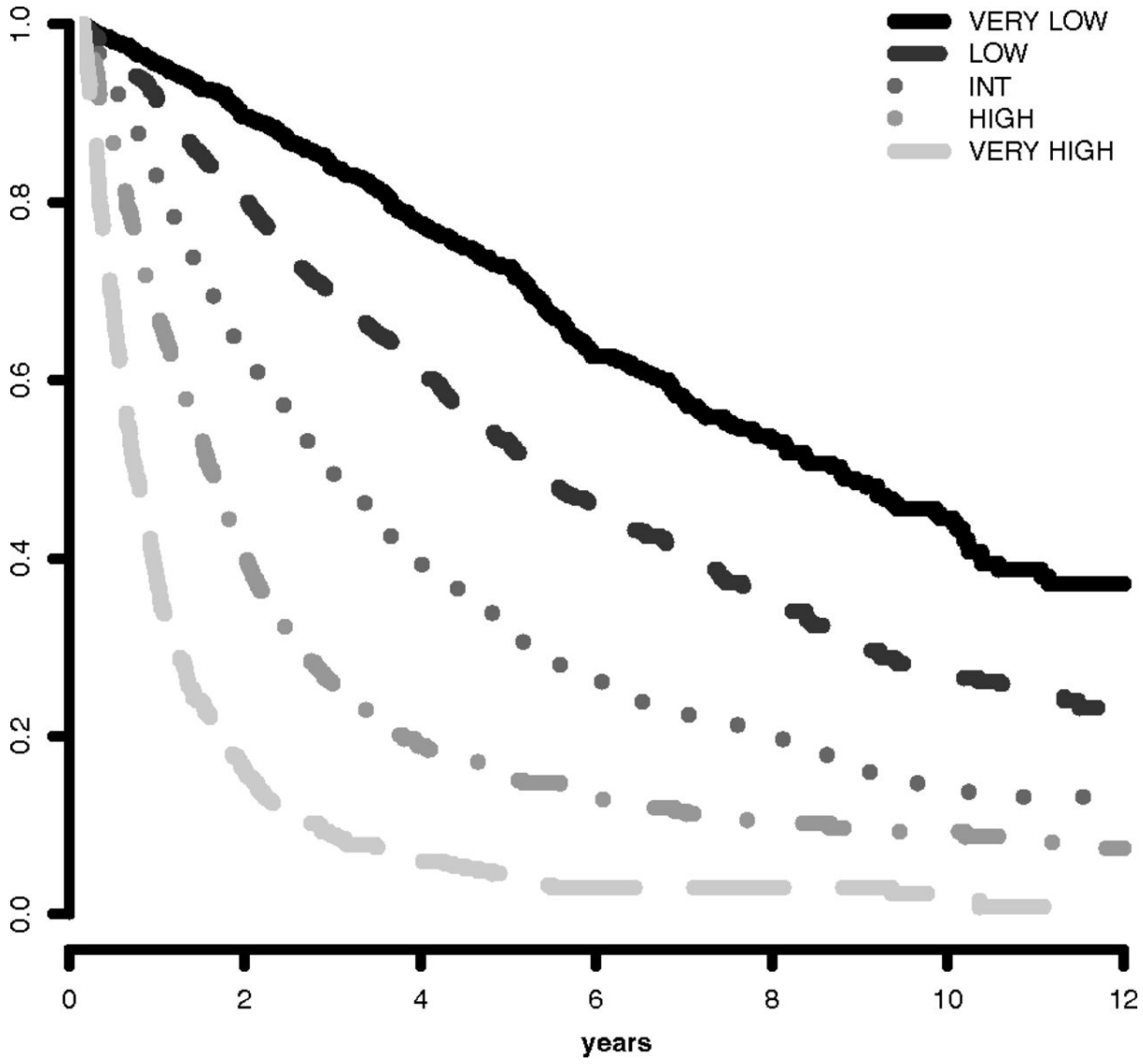
Prognostic Variable	Prognostic Score Value						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good	--	Good	--	Intermediate	Poor	Very poor
BM blast, %	≤ 2	--	> 2 to < 5	--	5-10	> 10	--
Hemoglobin, g/dL	≥ 10	--	8 to < 10	< 8	--	--	--
Platelets, x 10^9/L	≥ 100	50 to < 100	< 50	--	--	--	--
ANC, x 10^9/L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