ONCONOVA THERAPEUTICS

TARGETING CANCER, PROTECTING HEALTHY CELLS

Corporate Update Presentation

Biotech Showcase 2018

January 9 |San Francisco, CA

Nasdaq: ONTX

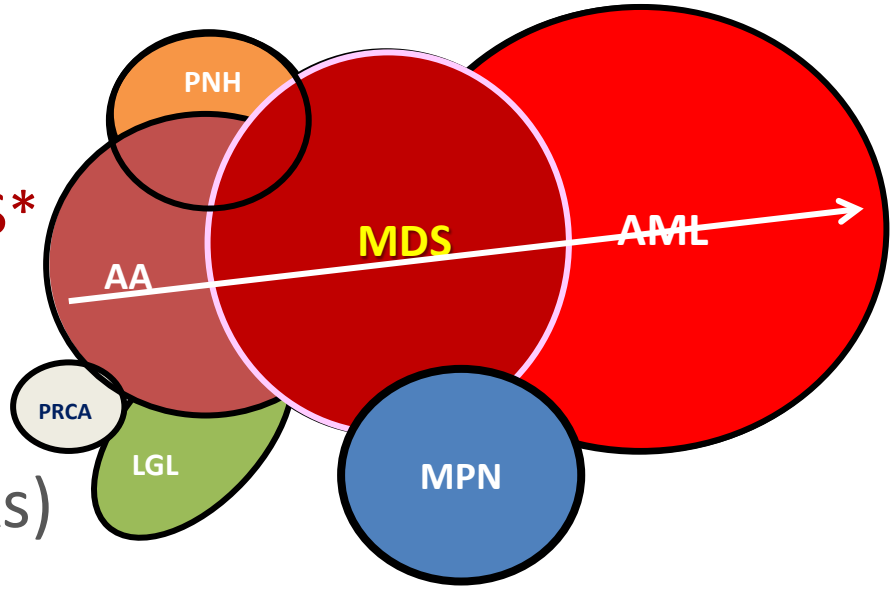
This presentation contains forward-looking statements about Onconova Therapeutics, Inc. based on management's current expectations which are subject to known and unknown uncertainties and risks. Onconova has attempted to identify forward-looking statements by terminology including "believes," "estimates," "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 in 1998; IPO in 2013 (Nasdaq: ONTX)
- Phase 3 stage clinical candidate: rigosertib
  - Targets RAS effector pathways (Cell, 2016)*
  - Focused on Myelodysplastic Syndromes (MDS)
- Rigosertib partnered with SymBio in Japan/Korea
  - Additional partnerships sought
- Broad pipeline with earlier stage drug candidates

MDS OVERLAPS WITH OTHER DISEASES

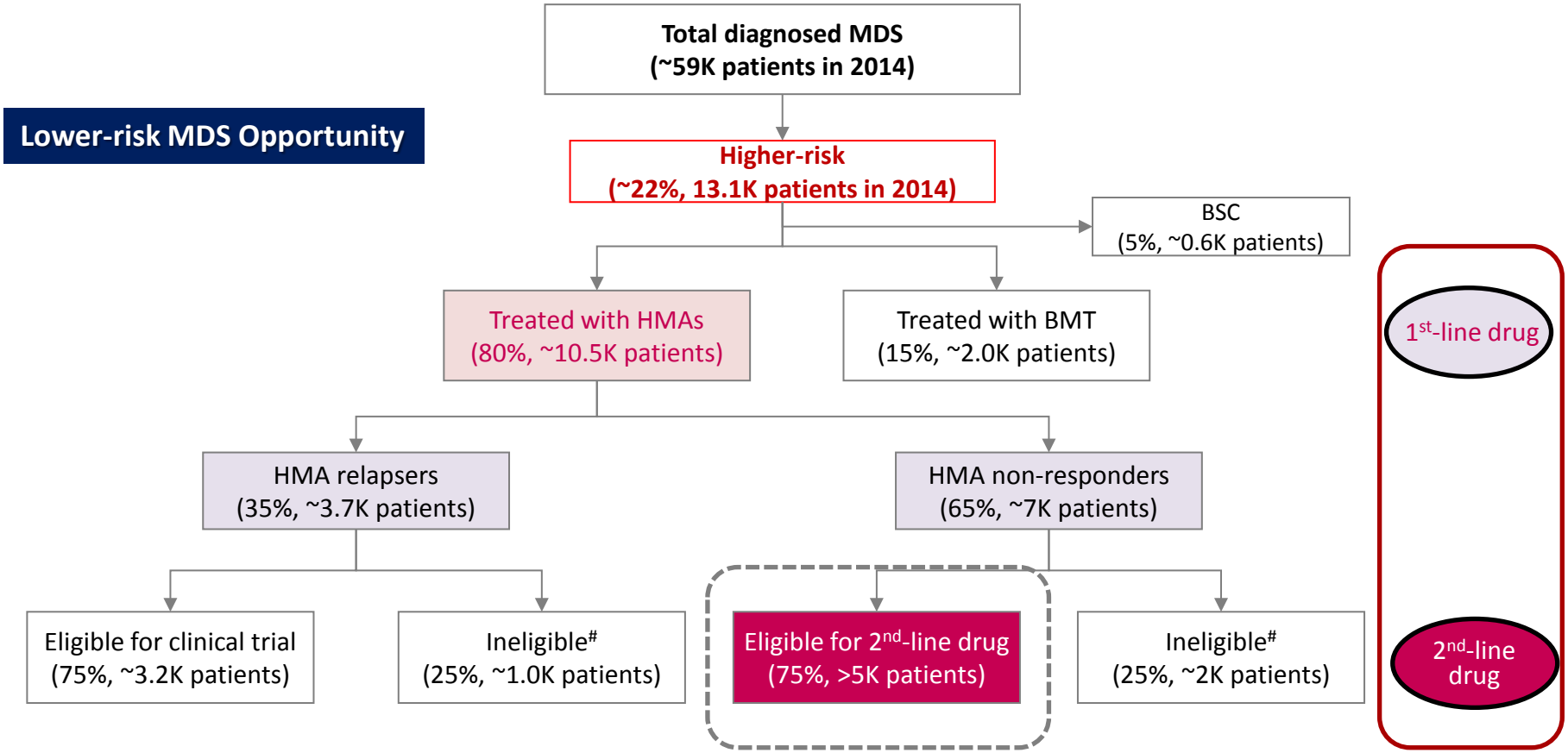
- MDS: malignant bone marrow disorder characterized by:[1]
  - Bone marrow failure leading to low blood counts
  - 30% of patients progress to AML
- US prevalence is 59,000
  - 18,000 have higher risk (HR) MDS*
  - ~10,000 second-line patients
- Treatment options limited to hypomethylating agents (HMAs)
  - Vidaza (Celgene); Dacogen (Eisai/J&J)
  - Approved >a decade ago; now off-patent



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

Slide credit: clinicaloptions.com

RIGOSERTIB IN MYELODYSPLASTIC SYNDROMES



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

ONCONOVA MDS FOCUS

Program	Partnership	Indication	Preclinical	Phase 1	Phase 2	Phase 3	NDA/MAA
Single-agent IV rigosertib	**Partnered with SymBio in Japan/Korea***	2nd-line Higher-risk (HR-MDS)	**INSPIRE Phase 3 Trial; Global trial running on 4 continents**				
Oral rigosertib + azacitidine		1st-line Higher-risk (HR-MDS)	**End of Phase 2 Meeting with FDA conducted, Phase 2 expansion underway**				

Key Trials

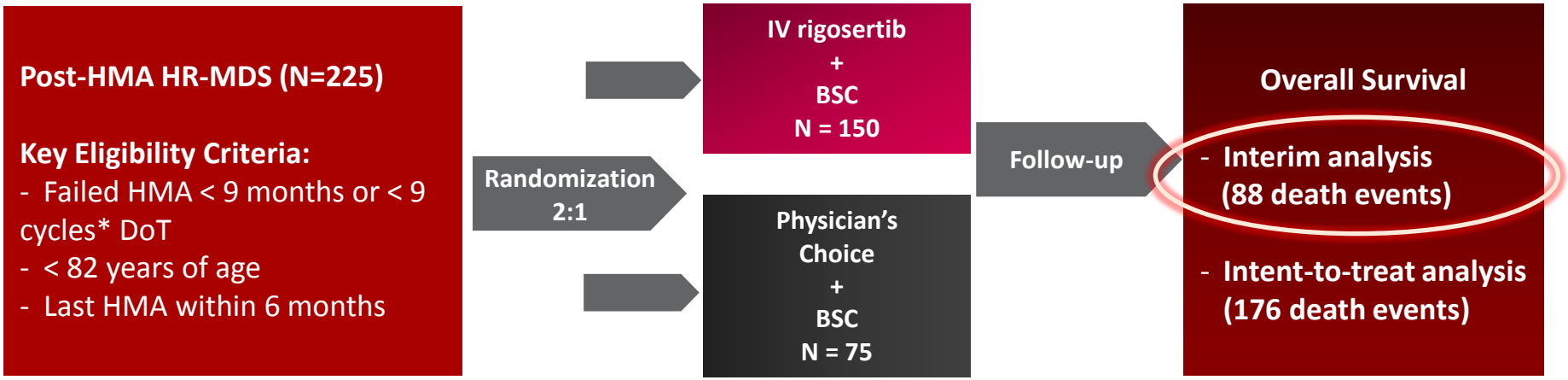
IV product for infusion

Oral soft gel capsules

LEAD INDICATION: RIGOSERTIB IN 2nd LINE HIGHER-RISK MDS

Advanced Phase 3-stage program

INSPIRE TRIAL DESIGN FOR GLOBAL PHASE 3 TRIAL



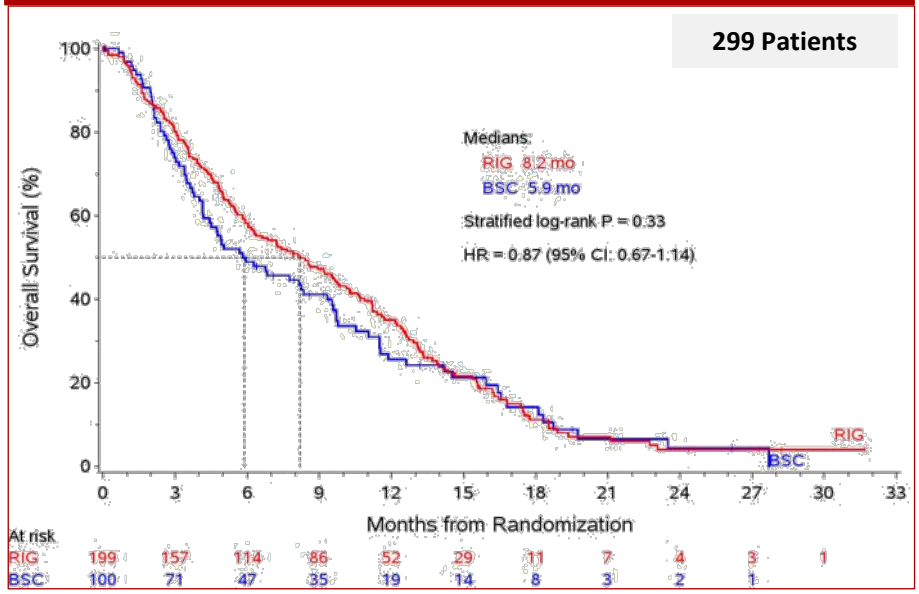
**9 cycles within 12 months of starting treatment*

- Survival endpoint with two successive analyses planned
  - ITT population enriched for higher-risk MDS
  - Second analysis of IPSS-Very High Risk (VHR) predefined group
    - Second cut allows for another chance to succeed in this subpopulation

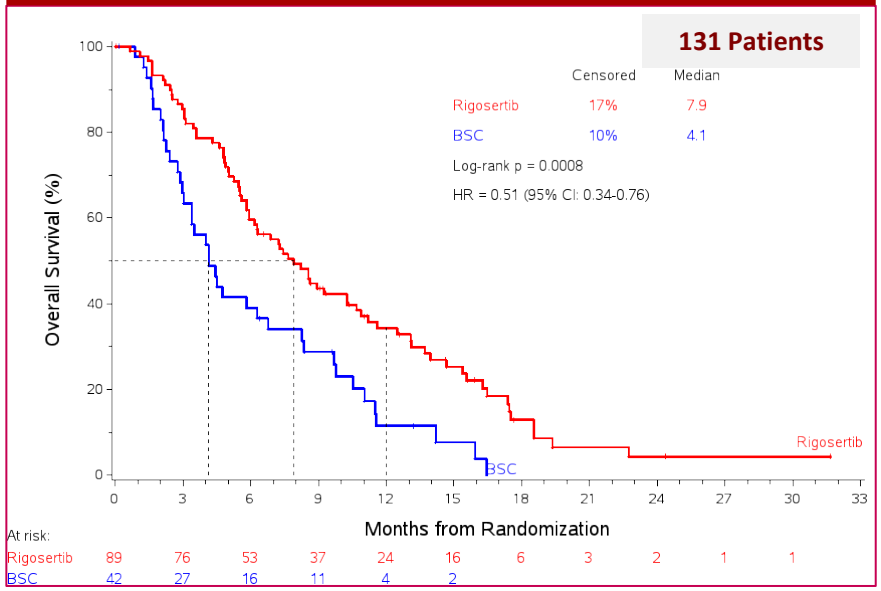
SELECTING PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

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

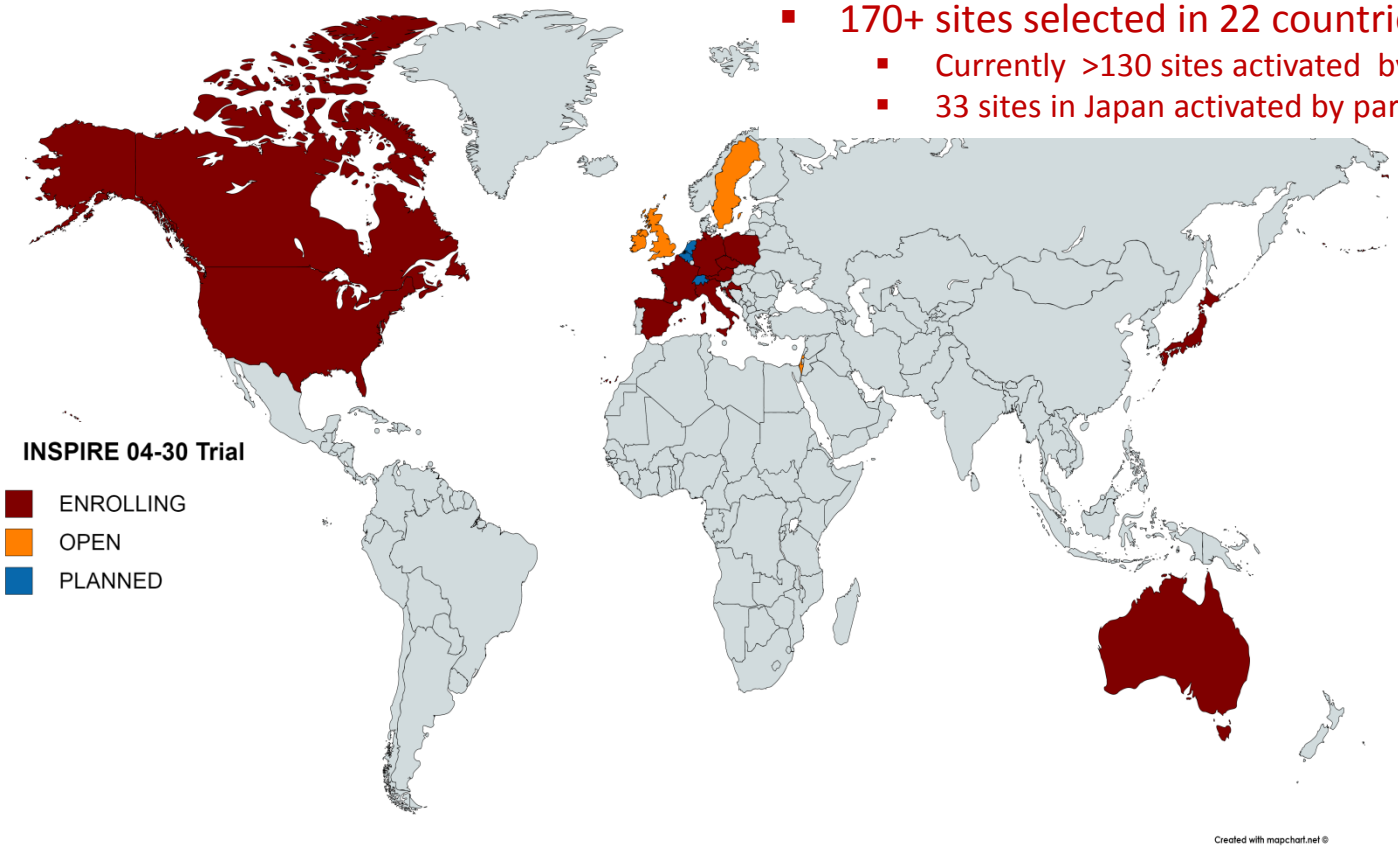
ITT OS of proposed INSPIRE population – HR = 0.51; P = 0.0008

**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*

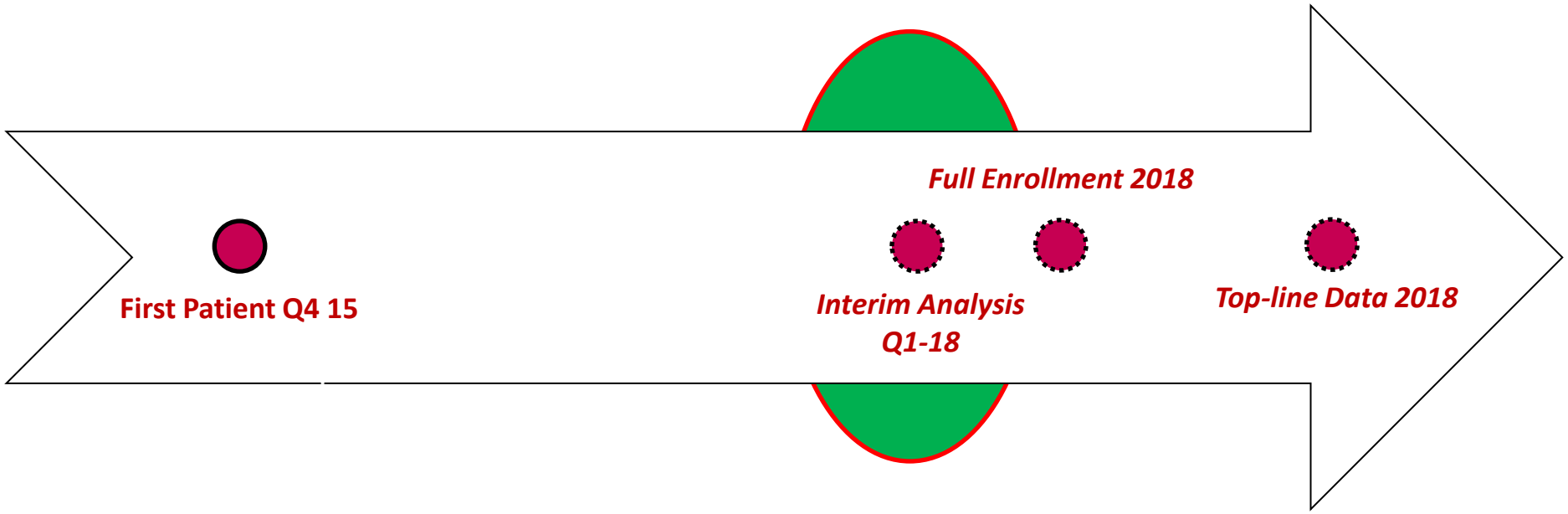
GLOBAL INSPIRE TRIAL PROGRESS

*The **IN**ternational **S**tudy of **P**hase III **IV** **R**igos**E**rtib, or INSPIRE, 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
- 170+ sites selected in 22 countries on 4 continents
  - Currently >130 sites activated by Onconova
  - 33 sites in Japan activated by partner SymBio



TIMELINES FOR DATA ANALYSIS FOR INSPIRE TRIAL

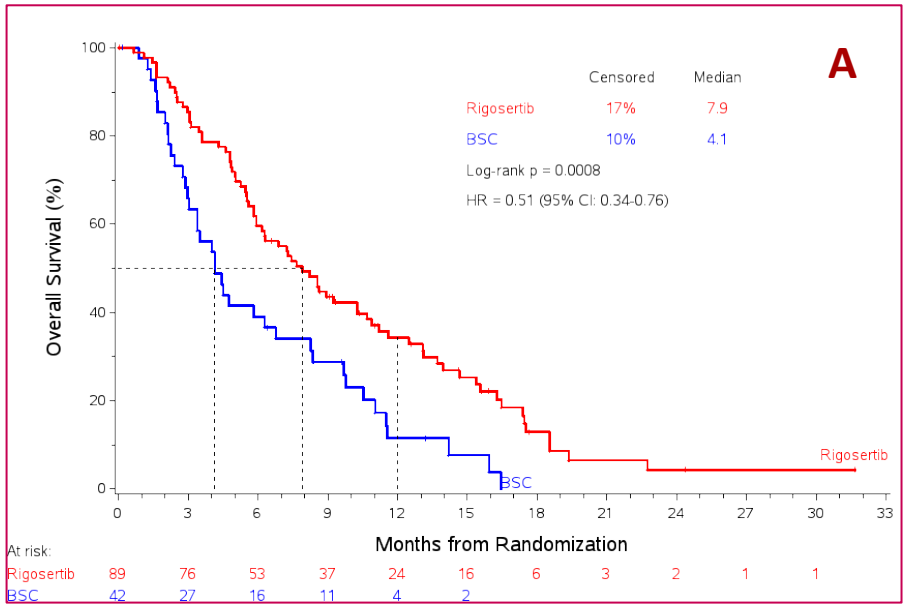


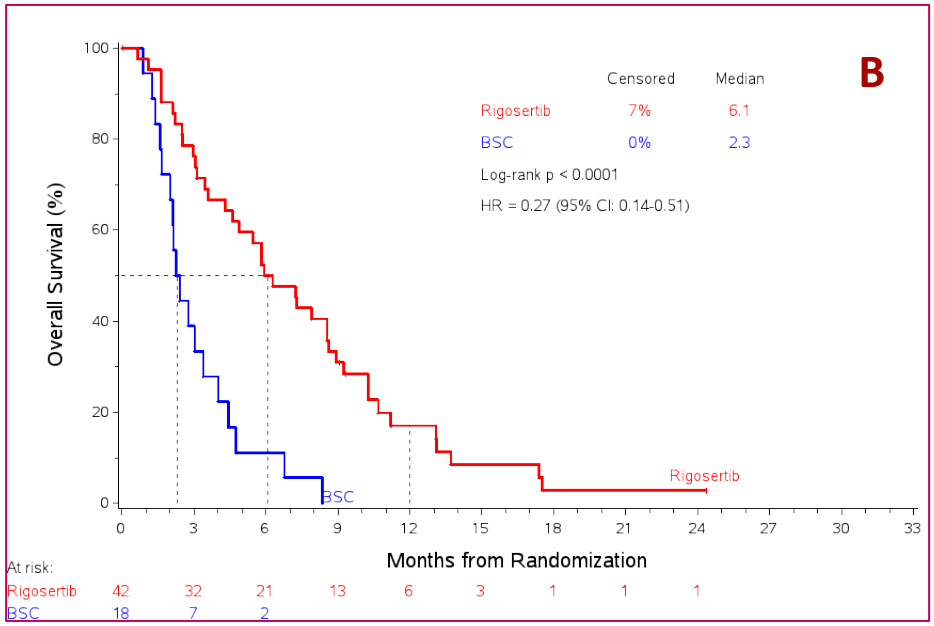
- Statistical analysis plan: two survival analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Two endpoints: OS in ITT population or IPSS-R Very High Risk*
- Exploratory genomic sequencing of patient samples

RETROSPECTIVE ANALYSIS OF SELECTED ITT POPULATION FOR INSPIRE

Post-hoc analysis of ONTIME patients (299 total enrolled) using INSPIRE enrollment criteria:

- A: Entire ITT population if new criteria were applied for patient selection
- B: Very High Risk (VHR) subgroup using new criteria





HR = 0.53; P 0.0008

HR = 0.27; P 0.0001

INSPIRE Trial Hypothesis: HR 0.625: P 0.04 for ITT; P 0.01 for VHR

UPCOMING INTERIM ANALYSIS

- Adaptive trial design to permit multiple choices
  - Efficacy and safety analysis conducted behind a firewall
  - Statistical Analysis Plan (SAP) after FDA and EMA consultation
  - Committee makes decisions based on data and pre-specified criteria
- Analysis after 88 events have occurred
  - Analysis results expected in January 2018
- Potential outcomes
  - Continue without modifications
  - Expand study to increase power using preset criteria
  - Focus on the Very High Risk pre-specified subgroup
  - Stop for futility
- Disclosure of enrollment and remaining timelines

COMBINATION THERAPY WITH RIGOSERTIB IN MDS

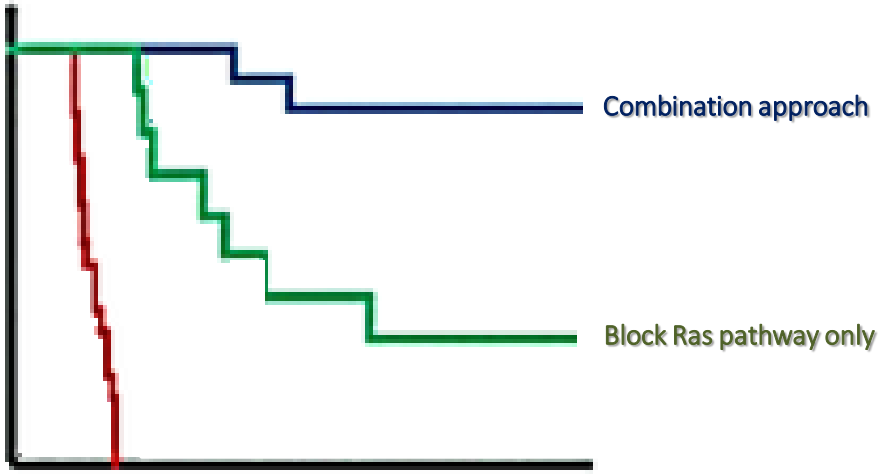
Phase 2 stage, expect to advance to Phase 3 in 2018

MECHANISTIC RATIONALE FOR COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

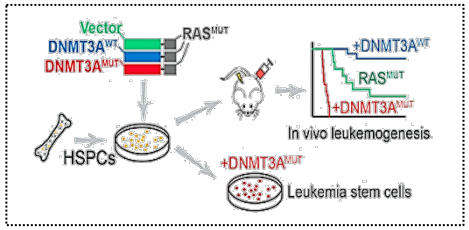
Preclinical evidence supports synergism of rigosertib + azacitidine combination

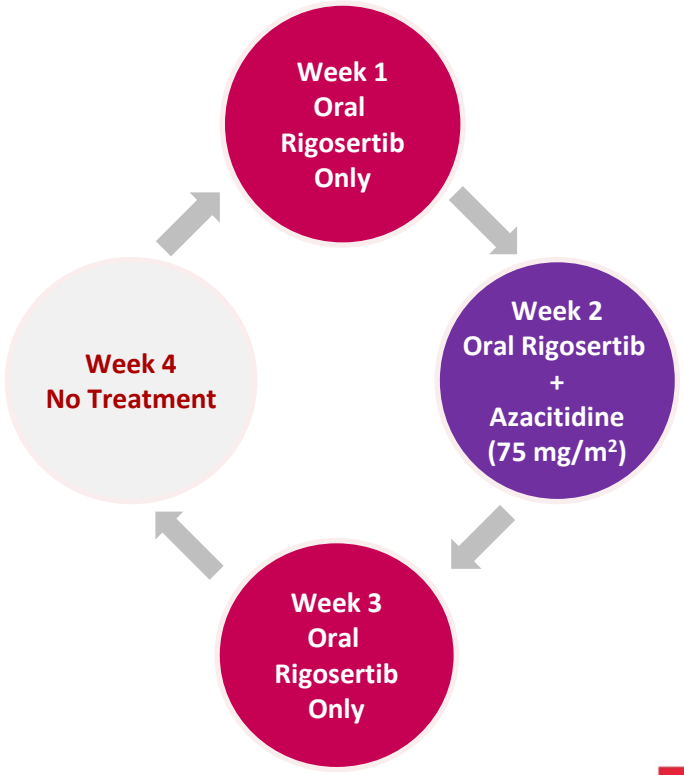
AML Animal Model

Validation of combination approach



Lu et al., 2016 *Cancer Cell*





More than 80 patients enrolled

EFFICACY RESULTS FOR COMBINATION TRIAL

An additional ~40 patients are currently being enrolled in the expanded Phase 2 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
Trial Start	2018	After regulatory discussions are completed

- Phase 2 trial expanded
  - Up to 40 more patients in multiple US sites
  - Dose and schedule optimization and to gain additional efficacy data
  - Enrollment proceeding briskly
- Phase 3 protocol synopsis created
- Scientific advice obtained from EMA

- FDA Special Protocol Assessment process to start after completing expansion

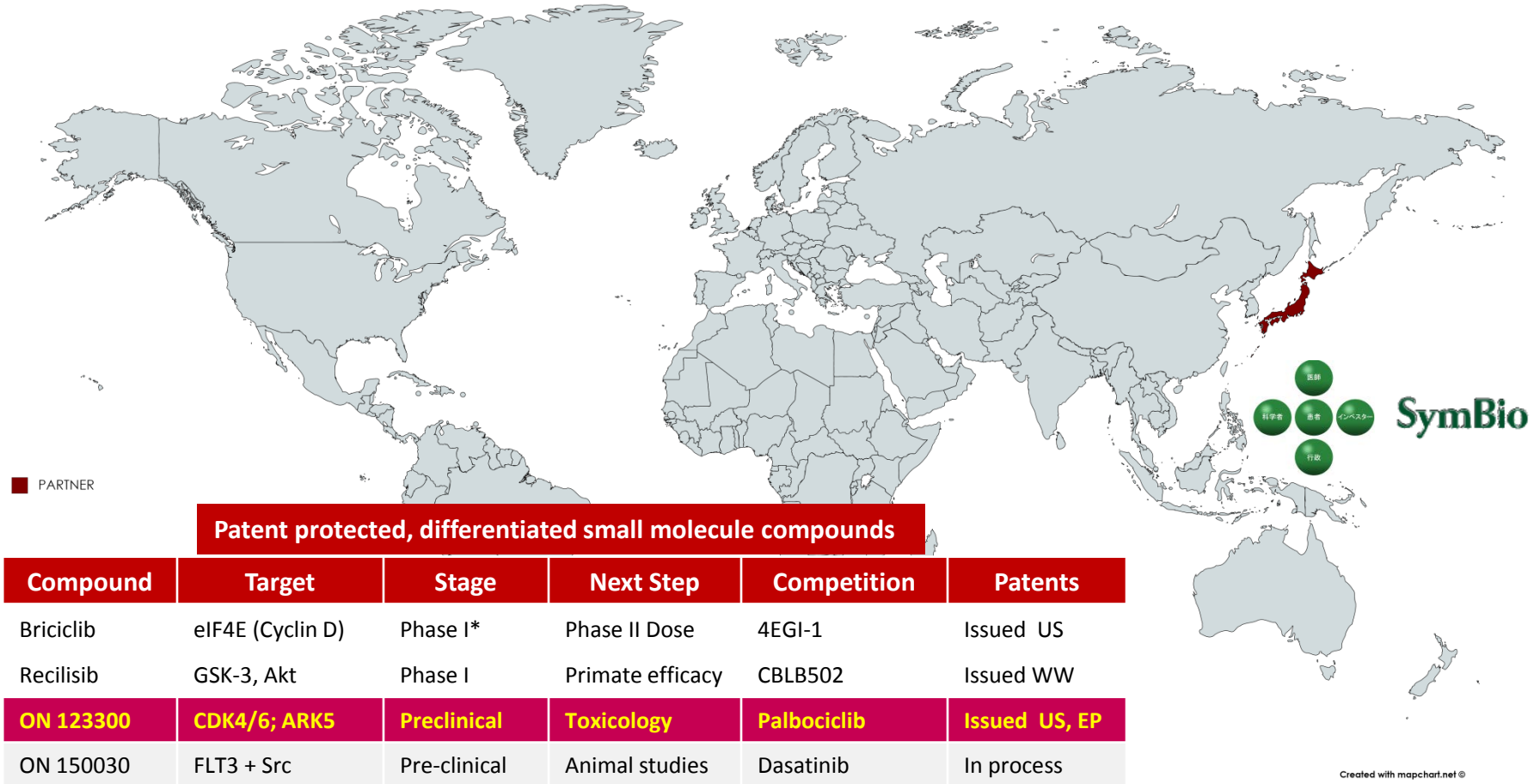
OTHER OPPORTUNITIES IN EARLY DEVELOPMENT

Collaborative programs

BUSINESS DEVELOPMENT OPPORTUNITIES:

RIGOSERTIB IS PARTNERED IN JAPAN/KOREA SINCE 2011

Partnerships for pipeline products sought in other territories



Patent protected, differentiated small molecule compounds

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 PROGRAM: NEXT GENERATION CDK INHIBITOR

Current generation CDK inhibitors

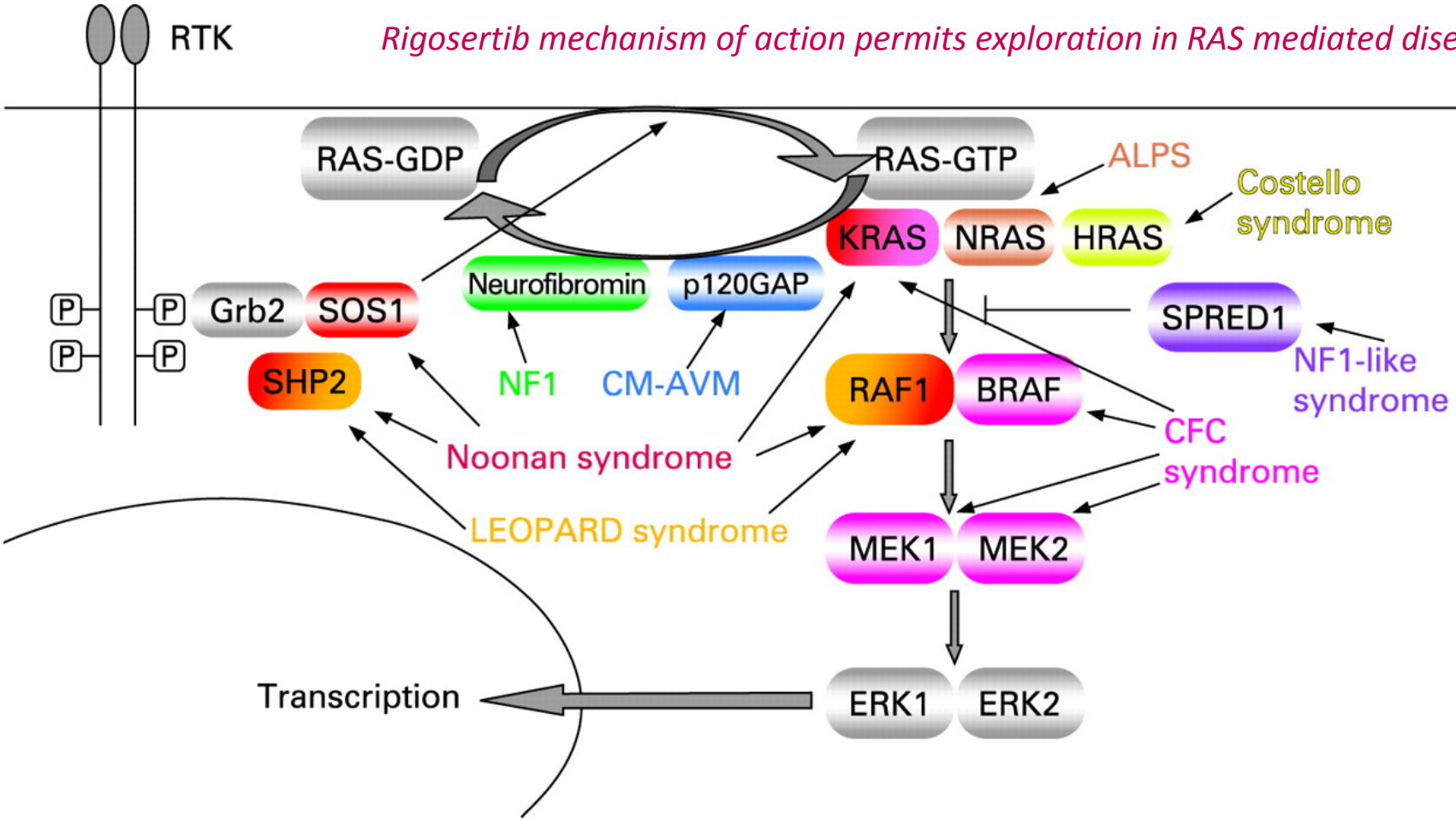
- Recently launched IBRANCE® (Palbociclib, Pfizer), Kisquali® (Ribociclib, Novartis) and Verzenio® (Abemaciclib, Lilly) have been considered to be potential breakthroughs in cancer therapy
  - First FDA approval for breast cancer
  - Target CDK4/6
- ON 123300 differentiated features
  - In addition to CDK4/6 also targets ARK5 controlling cellular metabolism and survival
  - Potential to act as single agent
  - Potential to affect emergence of resistance (RB-negative setting)
  - Differentiated pre-clinical efficacy
  - Blood-brain barrier penetrating properties

Partnership with HanX

- Announced December 19, 2017
- License for Greater China
  - Onconova retains ROW rights
- HanX to fund IND studies
  - HanX to file in China
  - Onconova to file in US
- Upfront, milestones, royalties
- HanX a specialty Oncology company
  - Phase 1 stage PD-1 antibody
  - Checkpoint blockade and CDK inhibition believed to be synergistic
- Next Milestone is IND

RASOPATHIES: CAUSATIVE MUTATIONS NOT LIMITED TO RAS IN RARE PEDIATRIC DISEASES

Rigosertib mechanism of action permits exploration in RAS mediated diseases



Collaborative research and development agreement (CRADA) signed with NIH in January 2018

FINANCIAL DETAILS & SUMMARY

Onconova founded in 1998; public since 2013

Ticker	Nasdaq ONTX	**Debt**	$0
Stock Information	▪ 10.8 million shares outstanding ▪ Public float >84% ▪ 52-week range: $1.36 - $3.22 ▪ 52-week average daily volume: 120,000 ▪ 4Q17 average daily volume: 198,000	**Liquidity**	▪ Cash and cash equivalents of $7.6 million as of 9-30-2017 (excluding Nov-17 raise of $1.4 million) ▪ S-3 effective Dec-17, S-1 filed Dec-17
Ownership	Tyndall, Tavistock, Sabby, Shire; insiders including management	**Burn-rate**	Average $5.6 million per quarter over the last 5 quarters
Analyst Coverage*	H.C. Wainwright, Laidlaw, Maxim, LifeSci Capital, Van Leeuwenhoeck Research (VLR). SeeThru Equity, Dawson James	**Partnerships**	▪ Rigosertib is partnered with SymBio Pharmaceuticals in Japan/Korea; Onconova retains rights to the rest of the world ▪ CDK 4/6 & ARK-5 compound partnered with HanX for Greater China

**Reports available upon request*

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 HIGHLIGHTS

- Company founded in 1998 and public since 2013 (Nasdaq: ONTX)
- Targeting underserved needs in Myelodysplastic Syndromes (MDS)
- Lead drug Rigosertib in Phase 3 "INSPIRE" trial for Higher-risk MDS
  - Currently no approved drugs for 2nd line patients
- Designing Phase 3 trial for Oral rigosertib + azacitidine combination

- Key upcoming milestones
  - INSPIRE (IV) Phase 3 interim analysis expected in **January 2018**
  - Full trial enrollment and Top-line Phase 3 data next key milestones

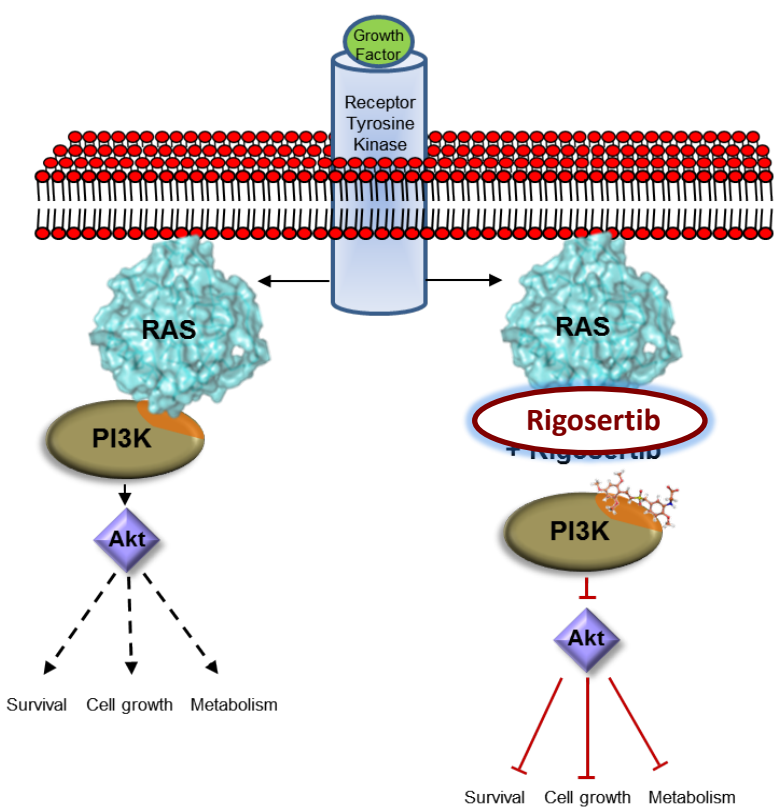
- Actively seeking partnerships
  - Rigosertib licensed to SymBio in Japan; other territories in discussion
  - High value preclinical stage next generation CDK4/6 inhibitor

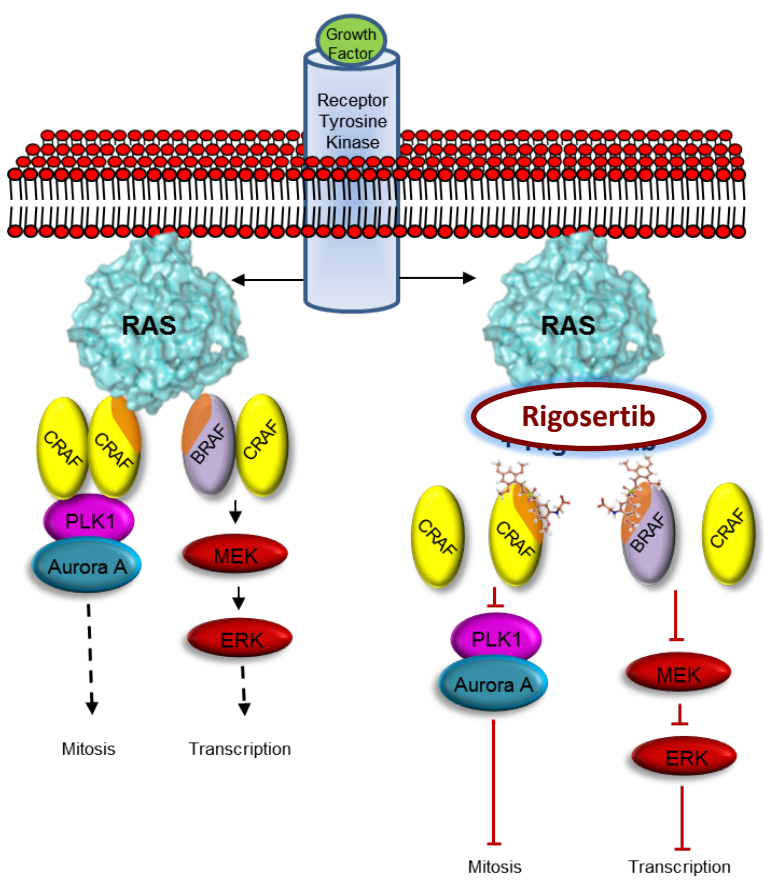

ONCONOVA
THERAPEUTICS
info@onconova.us

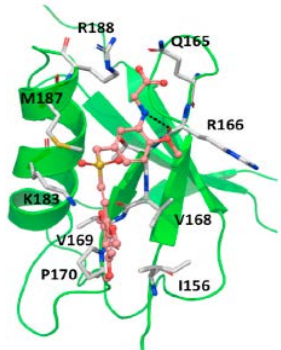
ADDITIONAL SLIDES

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







Rigosertib bound to Ras Binding Domain

Published in Cell, 2016

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 $\beta = 0.20$ (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

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

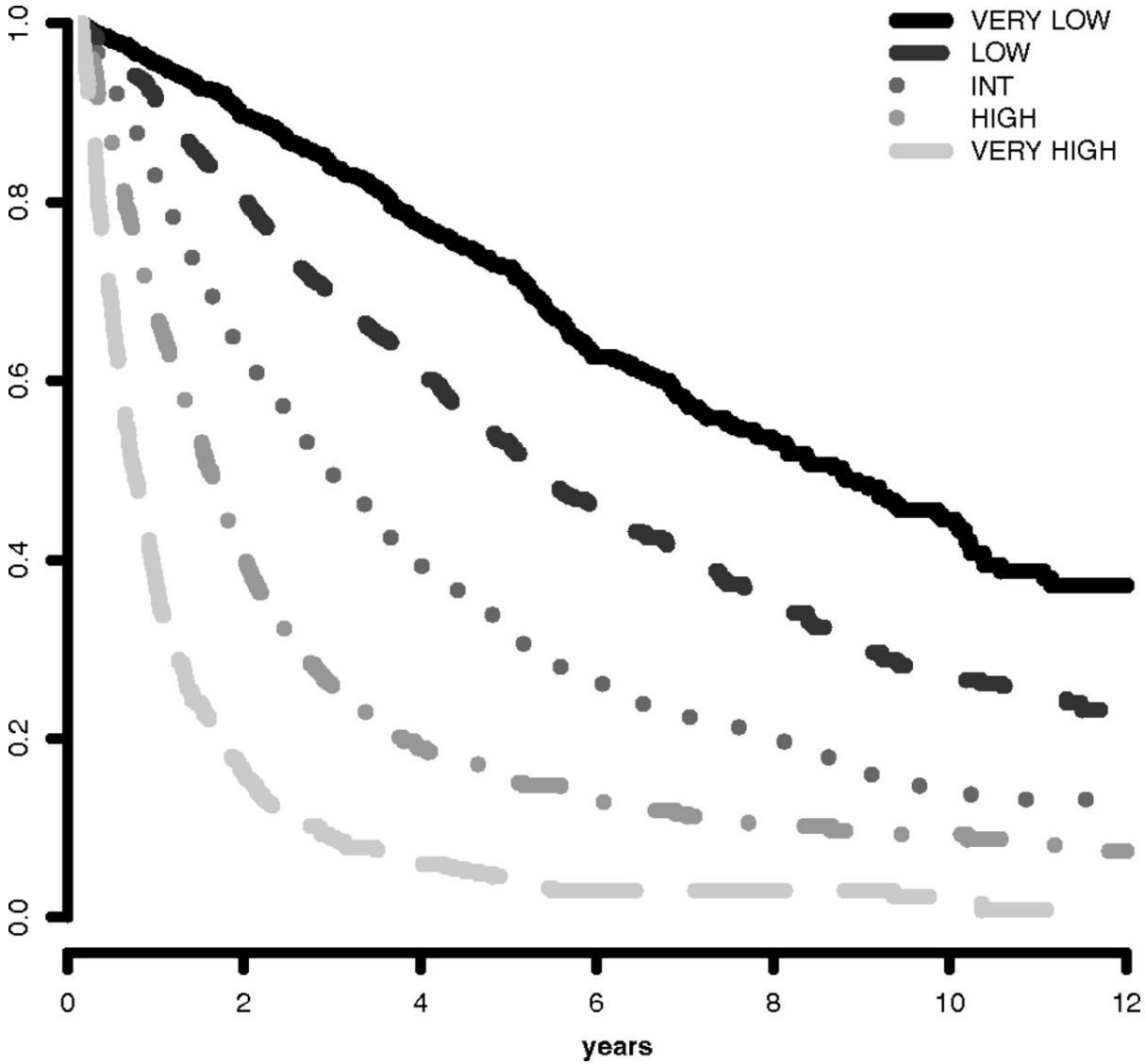
- **Maria R. Baer, MD - University of Maryland Greenebaum Cancer Center, Baltimore**
- Robert H. Collins, Jr., MD, FACP - University of Texas Southwestern Medical Center, Dallas
- **Guillermo Garcia-Manero, MD - University of Texas MD Anderson Cancer Center, Houston***
- **Lucy Godley, MD, PhD - University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

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

REVISED IPSS: PROGNOSTIC SCORE VALUES AND RISK CATEGORIES/SCORES

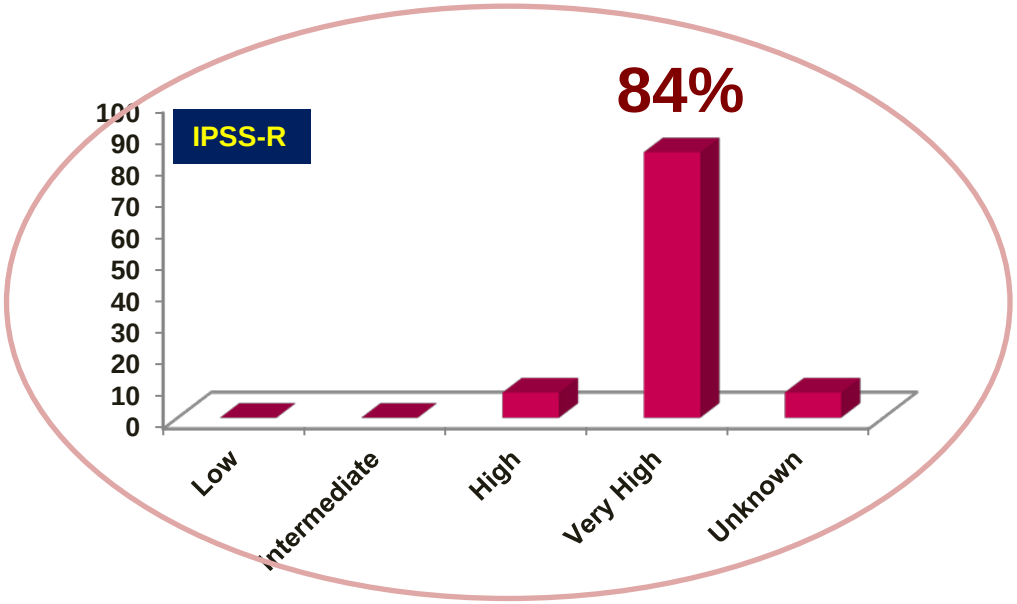
Prognostic Variable	Prognostic Score Value						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good	--	Good	--	Intermediate	Poor	Very poor
BM blast, %	≤ 2	--	> 2 to < 5	--	5-10	> 10	--
Hemoglobin, g/dL	≥ 10	--	8 to < 10	< 8	--	--	--
Platelets, x 10^9/L	≥ 100	50 to < 100	< 50	--	--	--	--
ANC, x 10^9/L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

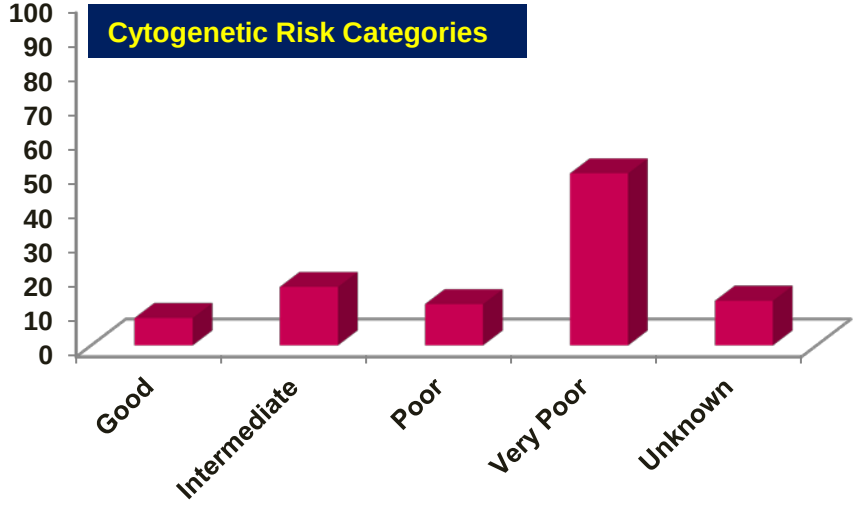
Risk	Score
Very low	≤ 1.5
Low	> 1.5 to 3.0
Intermediate	> 3.0 to 4.5
High	> 4.5 to 6.0
Very high	> 6

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

Slide credit: clinicaloptions.com

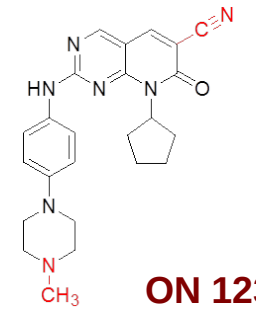
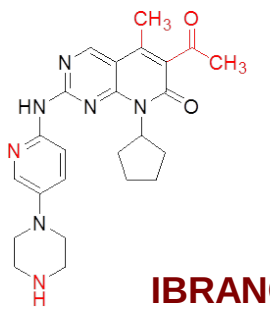
DISTRIBUTION (%) OF TP53 MUTATIONS BY PROGNOSTIC RISK CLASSIFICATION





- 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

DIFFERENTIATED KINASE INHIBITION: TARGETING OF ARK5

	Comparison of Two Compounds in Reaction Biology Kinase Assays	
	 **ON 123300**	 **IBRANCE®**

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

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

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