ONCONOVA THERAPEUTICS

TARGETING CANCER, PROTECTING HEALTHY CELLS

Corporate Update

BIO International Convention

June 20,2017, San Diego, CA

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

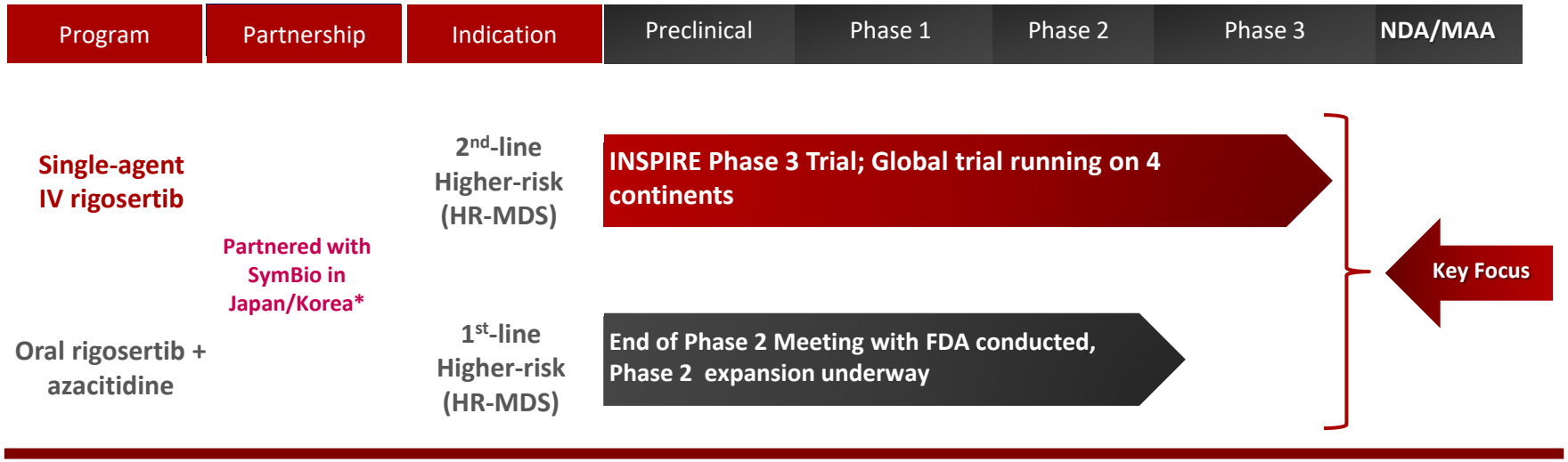
Key milestones upcoming in H2-2017 and 2018

FINANCIAL DETAILS

Onconova founded in 1998; public since 2013	
Ticker	Nasdaq ONTX
Stock information	▪ 9.9 million shares ▪ Public float >84% ▪ 52-week range $1.96 - $6.87 ▪ Average daily volume 116,000
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)*

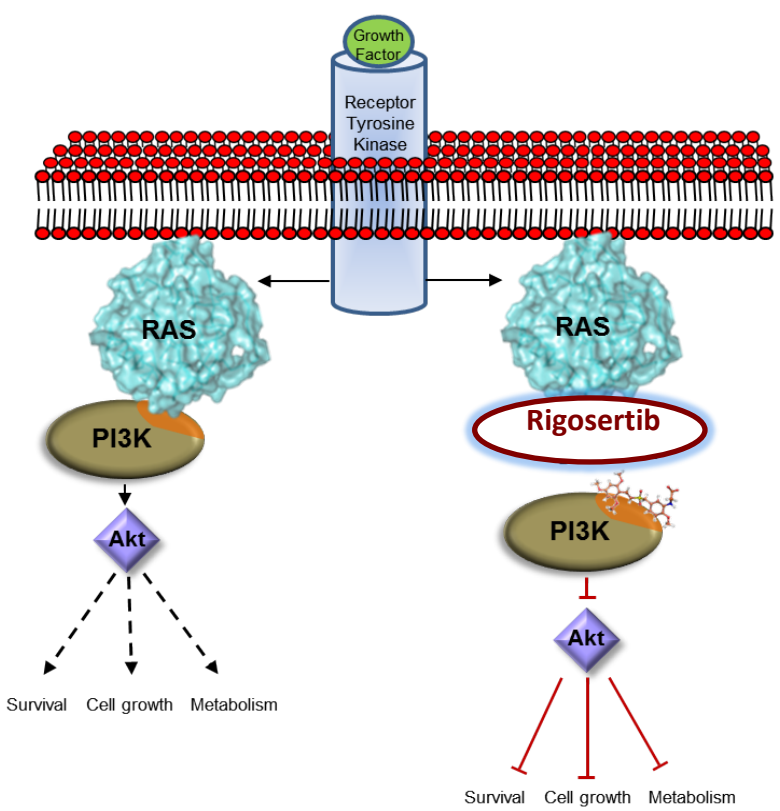
ONCONOVA MDS PIPELINE

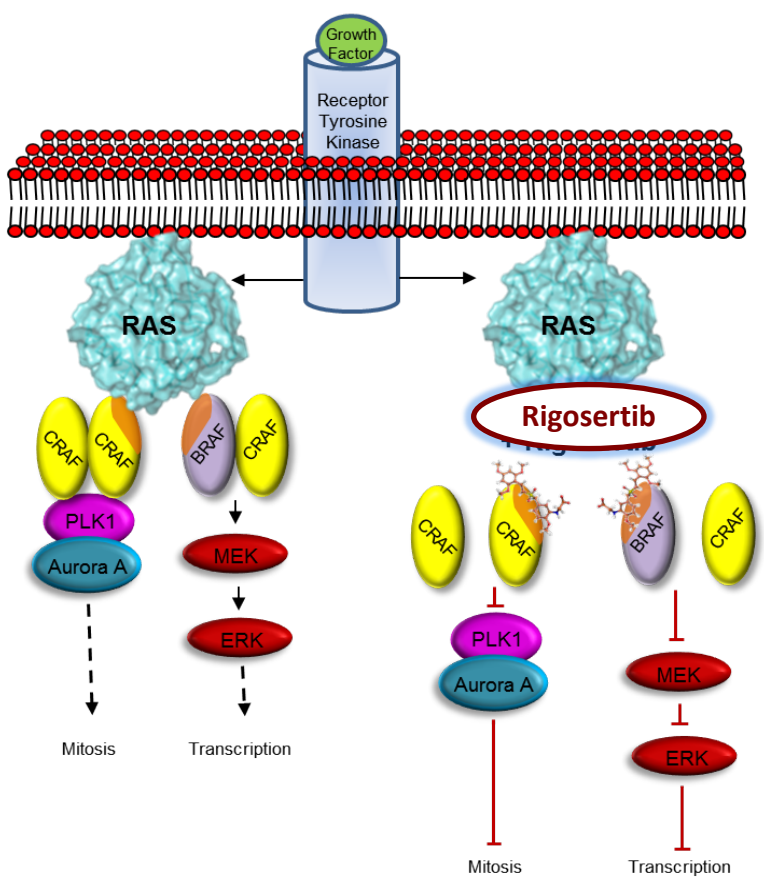


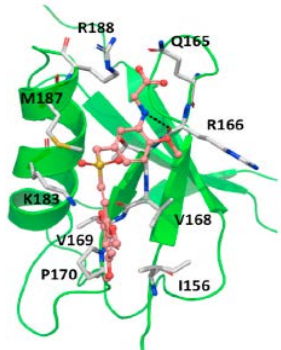
- More than 700 MDS patients have been treated in rigosertib Phase 1-3 trials
  - IV and Oral rigosertib, plus oral rigosertib combination with azacitidine
- Includes, in addition to Higher Risk MDS, Lower Risk, transfusion dependent patients
- New data on IV rigosertib:
  - Phase 2b 04-24 trial results were 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





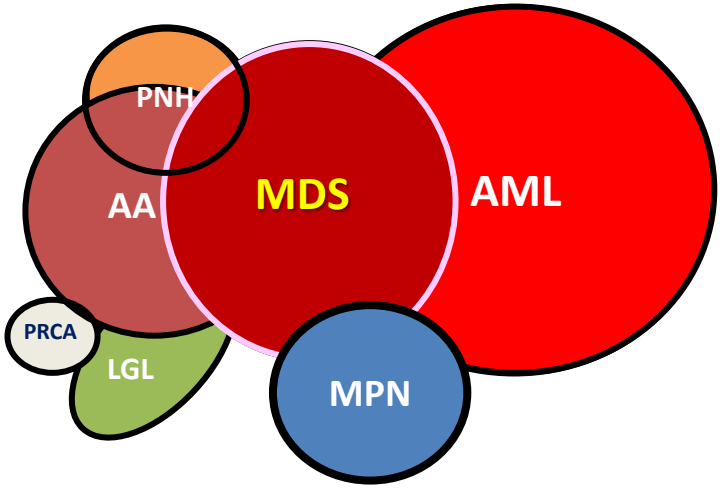


Rigosertib bound to Ras Binding Domain

Published in Cell, 2016

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
- No approved treatments for patient after HMA failure

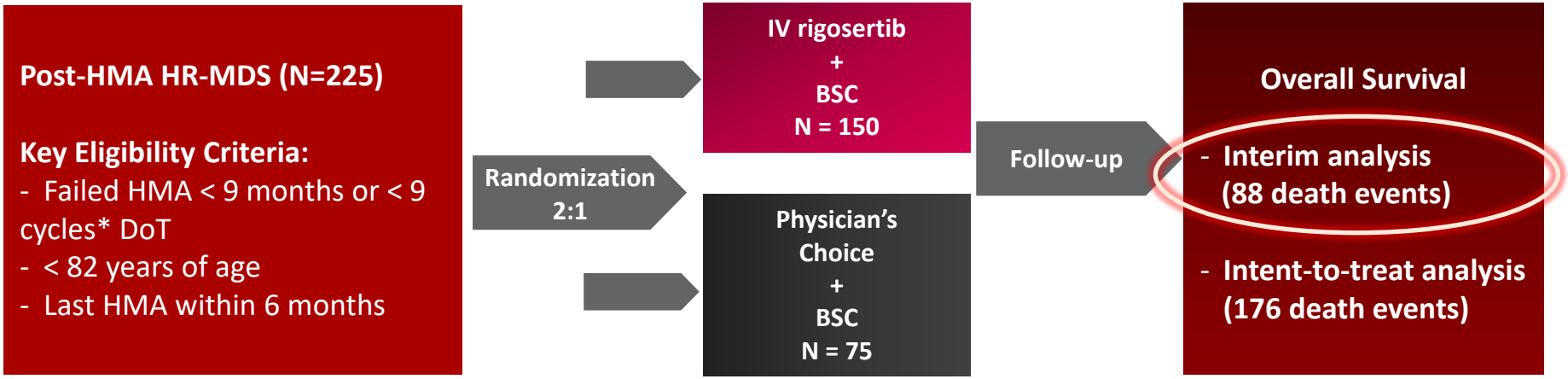


Slide credit: clinicaloptions.com

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

INSPIRE: GLOBAL PHASE 3 TRIAL

Targeted trial for selected patients who are not benefiting from HMA therapy



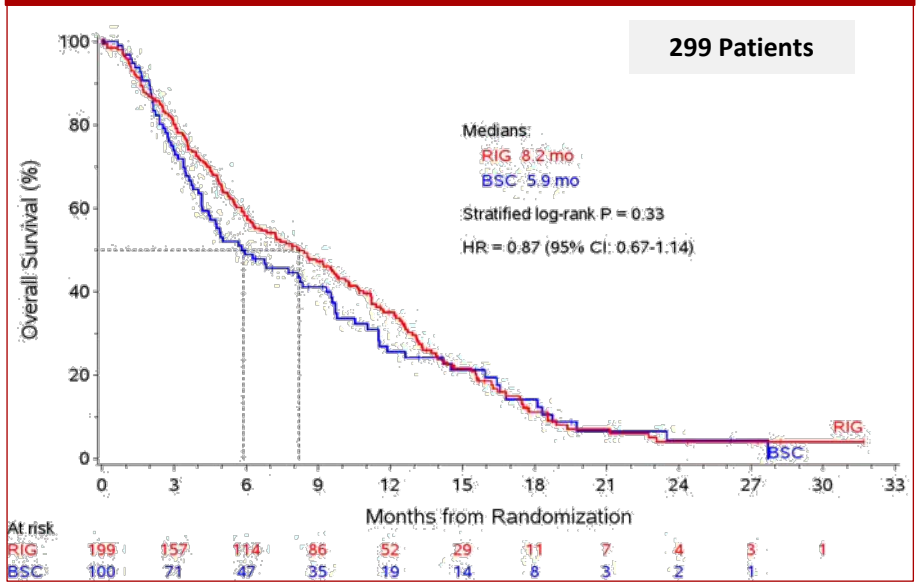
**9 cycles within 12 months of starting treatment*

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

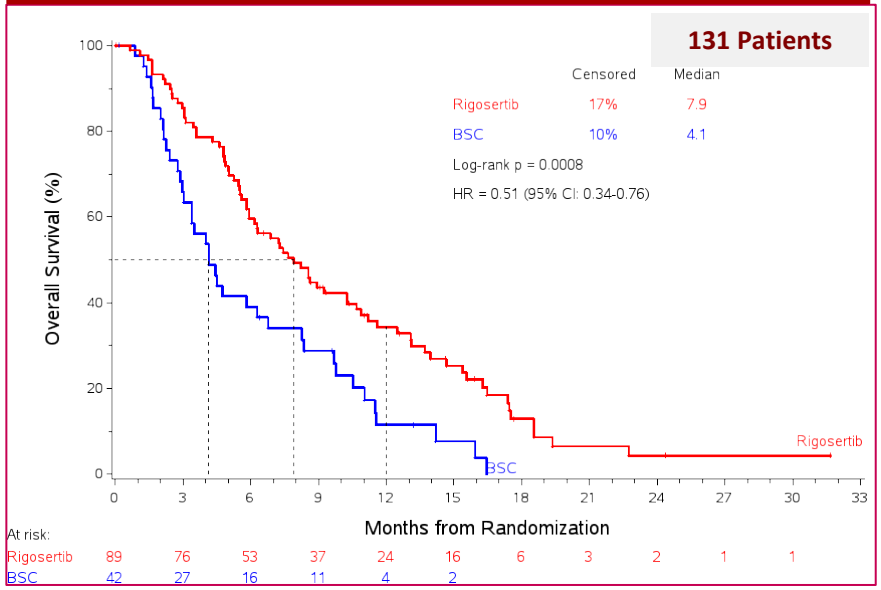
PATIENT POPULATION FOR PHASE 3 INSPIRE TRIAL

Data from ONTIME paper* published in *Lancet Oncology*

ITT for ONTIME Trial



Subpopulation for INSPIRE Trial (ONTIME subset)

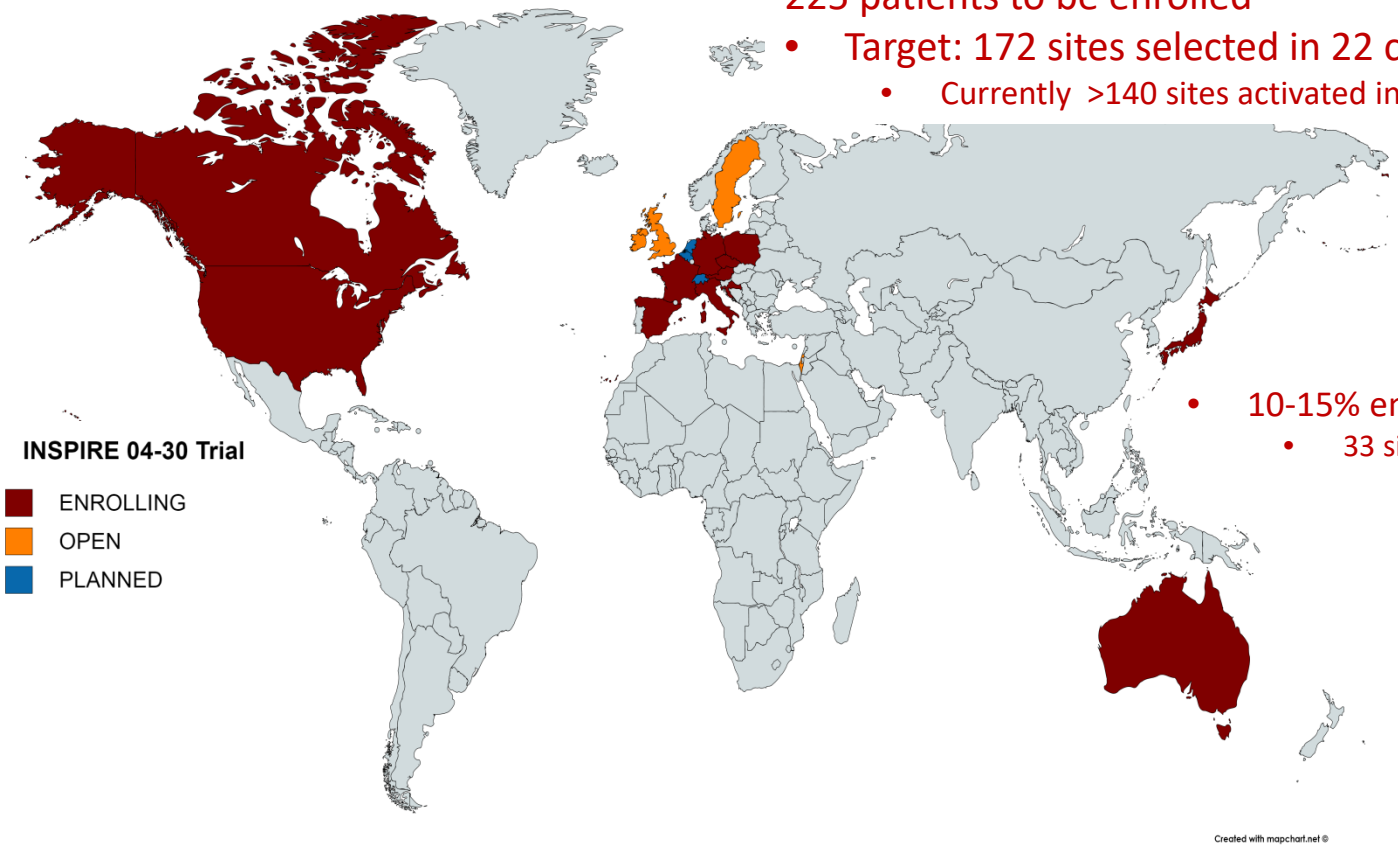


ITT OS analysis of ONTIME – HR= 0.87; NS survival benefit
ITT OS of proposed INSPIRE population – HR = 0.51; P = 0.0008

*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 **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

- Target: 172 sites selected in 22 countries on 4 continents
  - Currently >140 sites activated in 17 countries by Onconova

- 10-15% enrollment in Japan by SymBio
  - 33 sites in activated

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

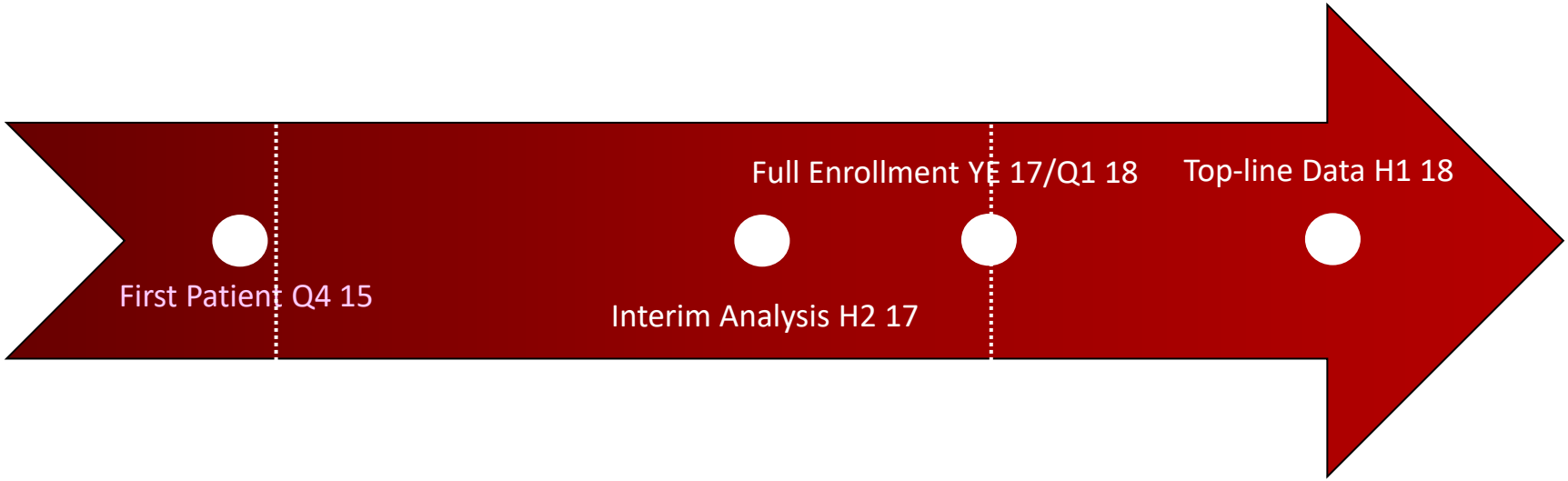
- **Maria R. Baer, MD - University of Maryland Greenebaum Cancer Center, Baltimore**
- Robert H. Collins, Jr., MD, FACP - University of Texas Southwestern Medical Center, Dallas
- **Guillermo Garcia-Manero, MD - University of Texas MD Anderson Cancer Center, Houston***
- **Lucy Godley, MD, PhD - University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

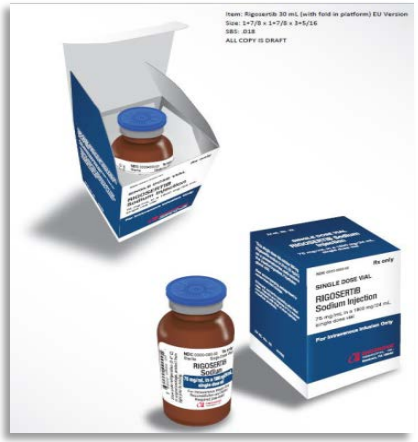
TIMELINES FOR DATA ANALYSIS FOR INSPIRE TRIAL

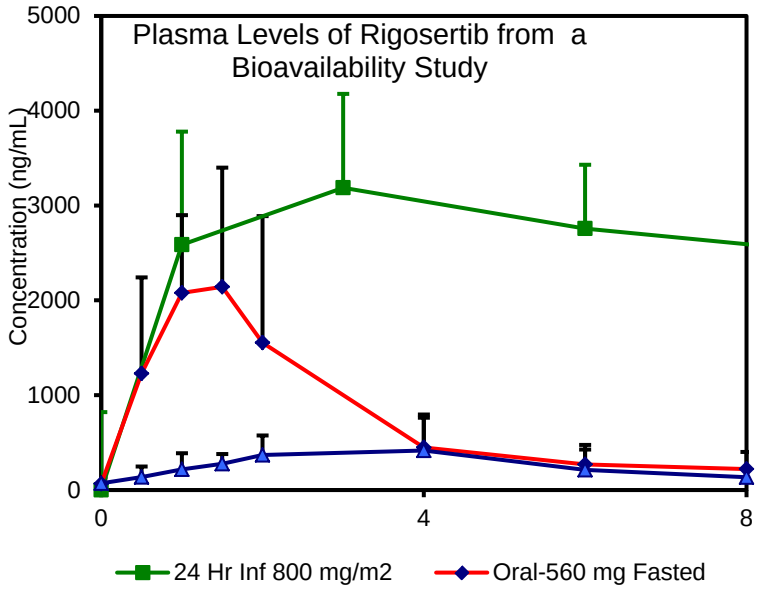


- Statistical analysis: two analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Dual primary endpoints: Overall survival in ITT population or IPSS-R Very High Risk
- Exploratory genomic sequencing of patient samples

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





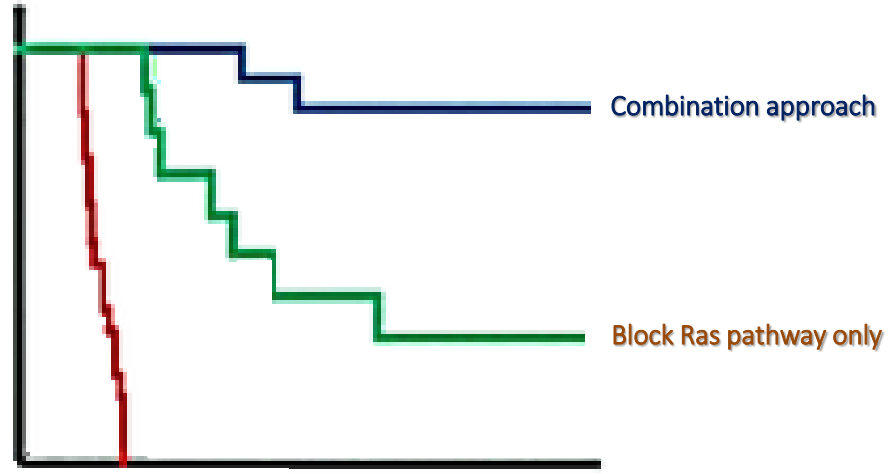
MECHANISTIC RATIONALE FOR COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

Preclinical evidence supports synergism of rigosertib + azacitidine combination

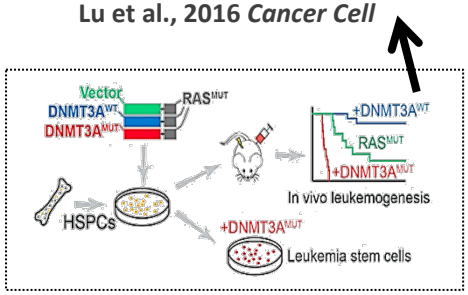
- Complexity of MDS
  - Defined by IPSS-R categories
  - Certain karyotypes
  - Different types of mutations
- DNA methylation changes
  - Addressed by HMA inhibitors
  - Early stage events
- Signal transduction changes
  - Later stage mutations
  - May be addressed by rigosertib
- Combination approach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

AML Animal Model

Validation of combination approach



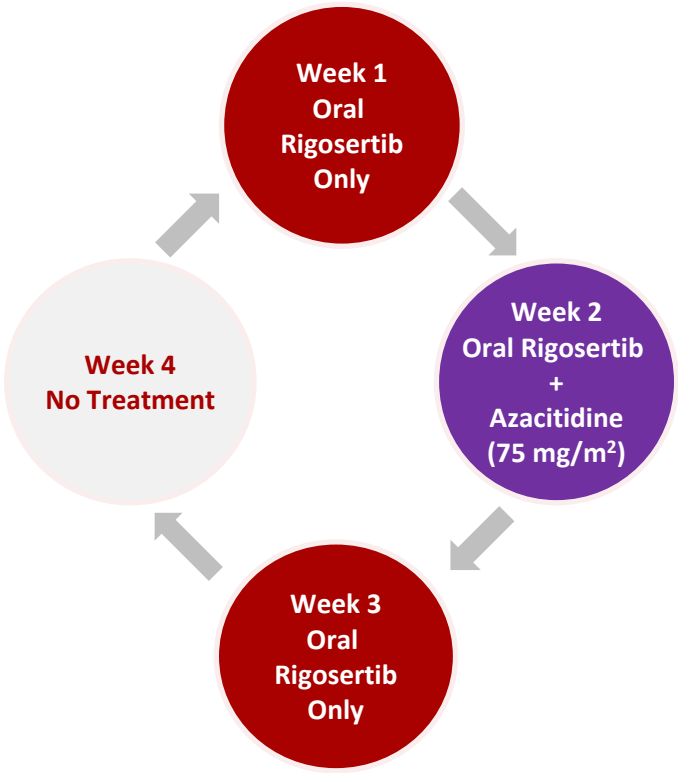
Lu et al., 2016 *Cancer Cell*



COMBINATION THERAPY PHASE 1/2 TRIALS

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 (data to be presented at EHA)
- 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

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

Azacitidine Package Insert[1]	
Adverse Event	Grade ≥3
Haematuria	2.3%
Anemia	13.7%
Neutropenia	61.1%
Thrombocytopenia	58.3%

Oral Rigosertib + Aza	
Adverse Event	Grade ≥3
Haematuria	7.0%
Anemia	0
Neutropenia	19.0%
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

[1]http://www.vidaza.com/pi.pdf

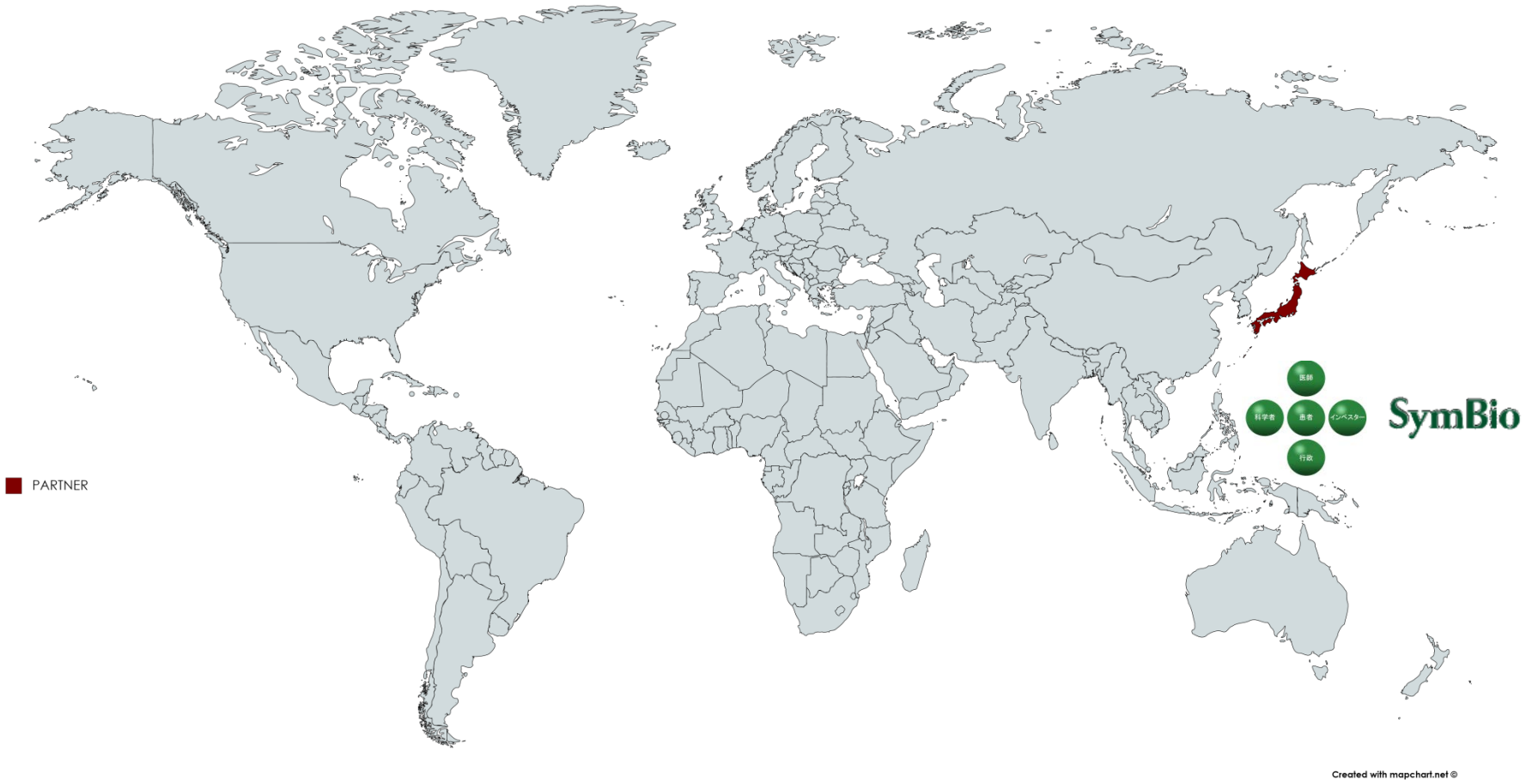
NEXT STEPS FOR RIGOSERTIB + AZACITIDINE DEVELOPMENT

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

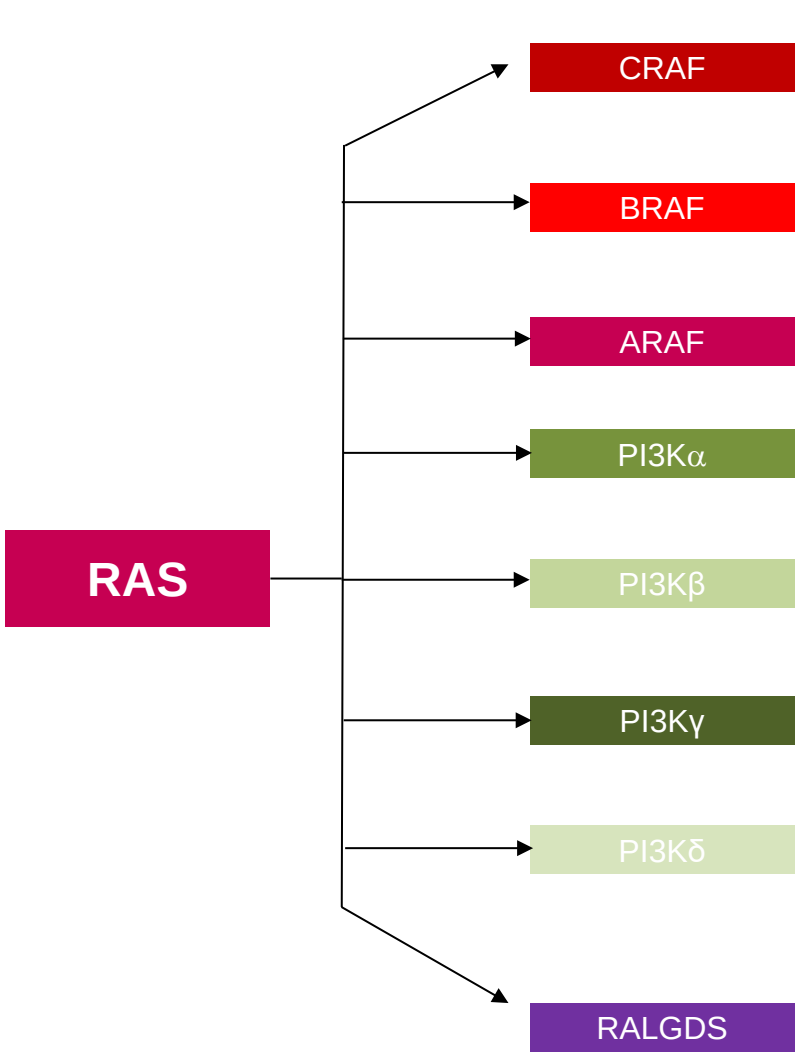
RIGOSERTIB IS PARTNERED IN JAPAN/KOREA SINCE 2011

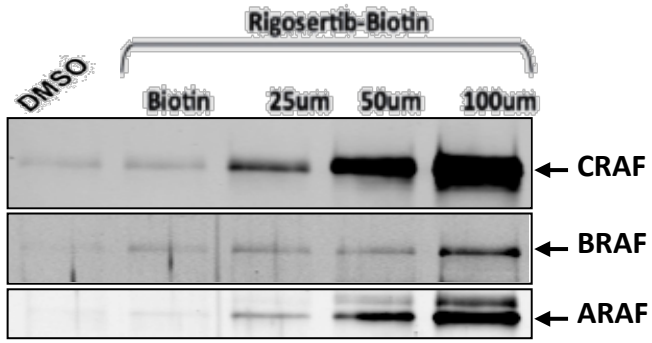


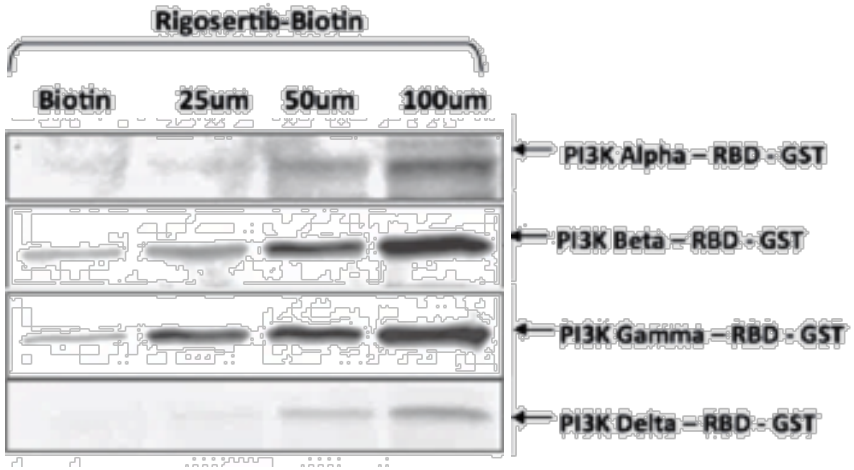
Partnerships sought in other territories

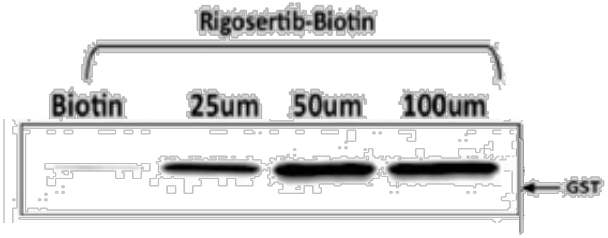
PROGRAMS BEYOND MDS AND RIGOSERTIB

RIGOSERTIB BINDS TO MULTIPLE RAS EFFECTOR RAS BINDING DOMAINS

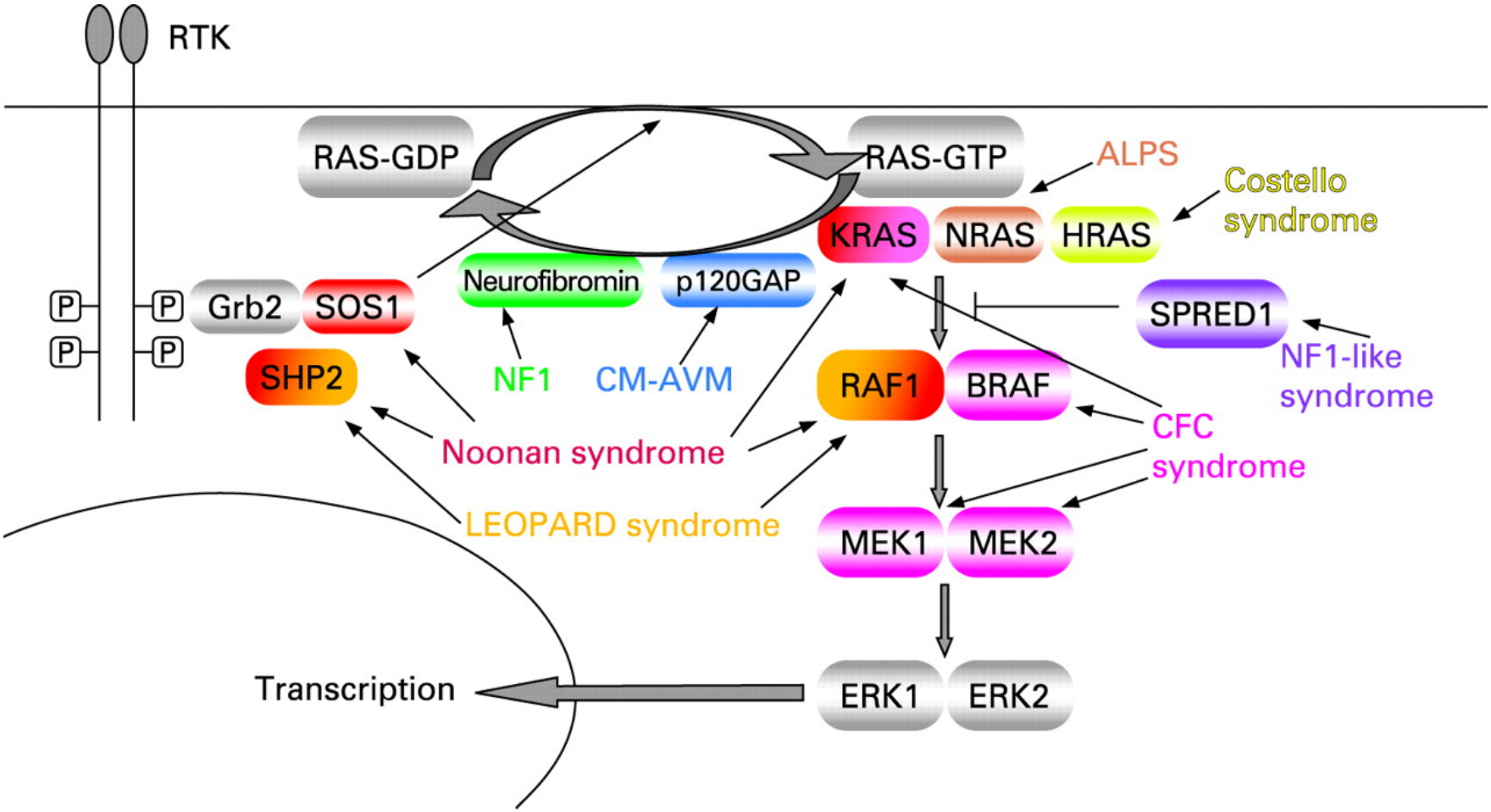








RASOPATHIES: CAUSATIVE MUTATIONS NOT LIMITED TO RAS



ONCONOVA PRODUCT CANDIDATE PIPELINE

Not including Rigosertib

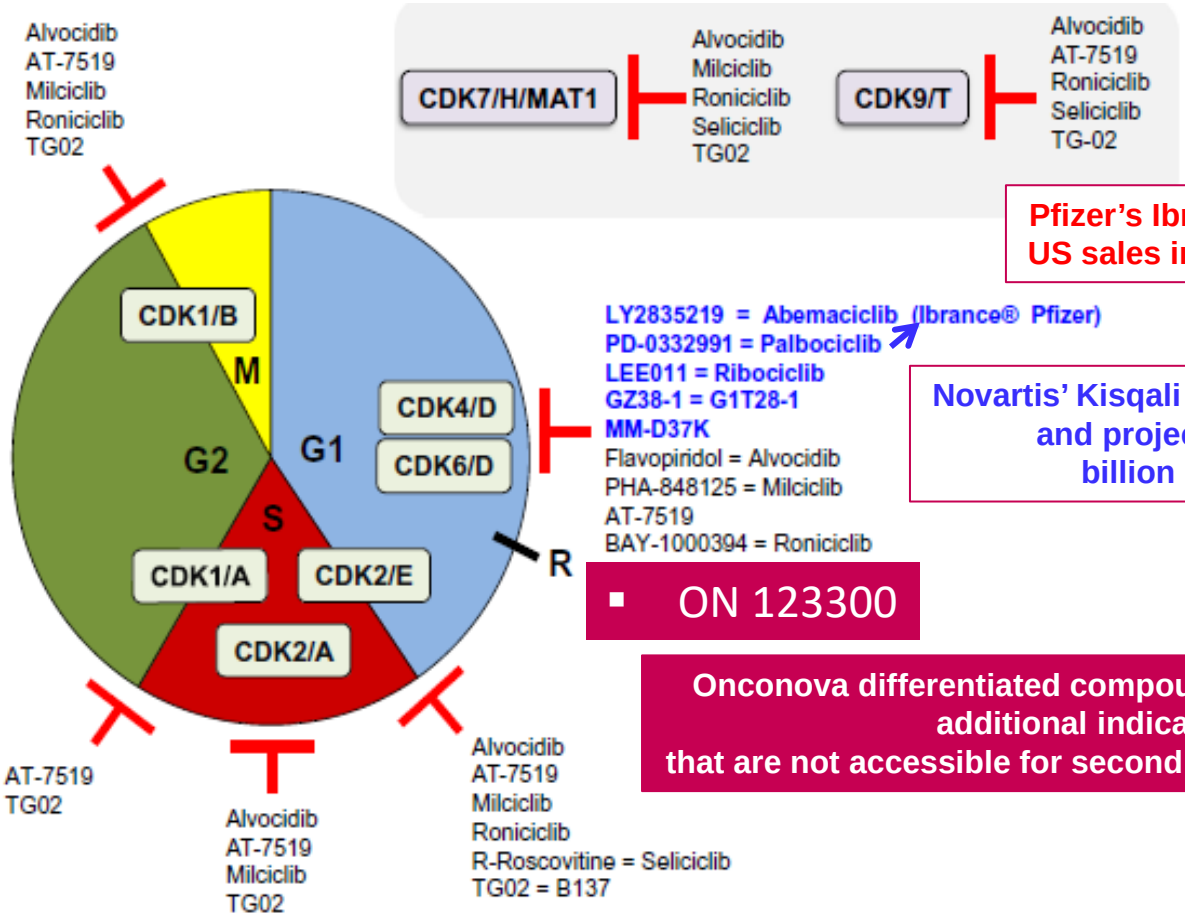
- Patent protected, differentiated small molecule compounds
- Partnerships sought for all programs

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*



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

- ON 123300

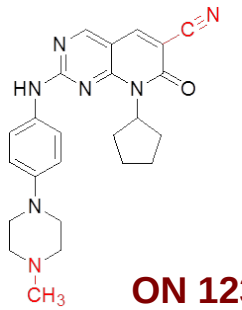
Onconova differentiated compound could be used for additional indications that are not accessible for second generation compounds

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

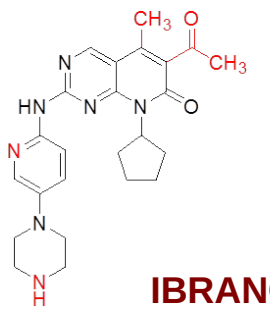
* C. Sánchez-Martínez et al./Bioorg. Med. Chem. Lett. 25 (2015) 3420–3435

DIFFERENTIATED KINASE INHIBITION THROUGH 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

ON 123300: SYNERGISTIC TARGETING OF CELL CYCLE *AND* METABOLIC PATHWAYS

- Targeting cell cycle (CDK4/6) together plus metabolic enzymes (ARK5)
  - Halts proliferation while starving cancer cell of energy required to expand
- ARK5, activated by Akt, which regulates survival & migration activity
- Co-targeting better approach than combination therapy

- Demonstrated differentiation of ON 123300
  - Rb-negative setting
  - Cytotoxicity
  - Apoptosis
  - Single agent activity

BRICICLIB: PHASE 1 STAGE NCE

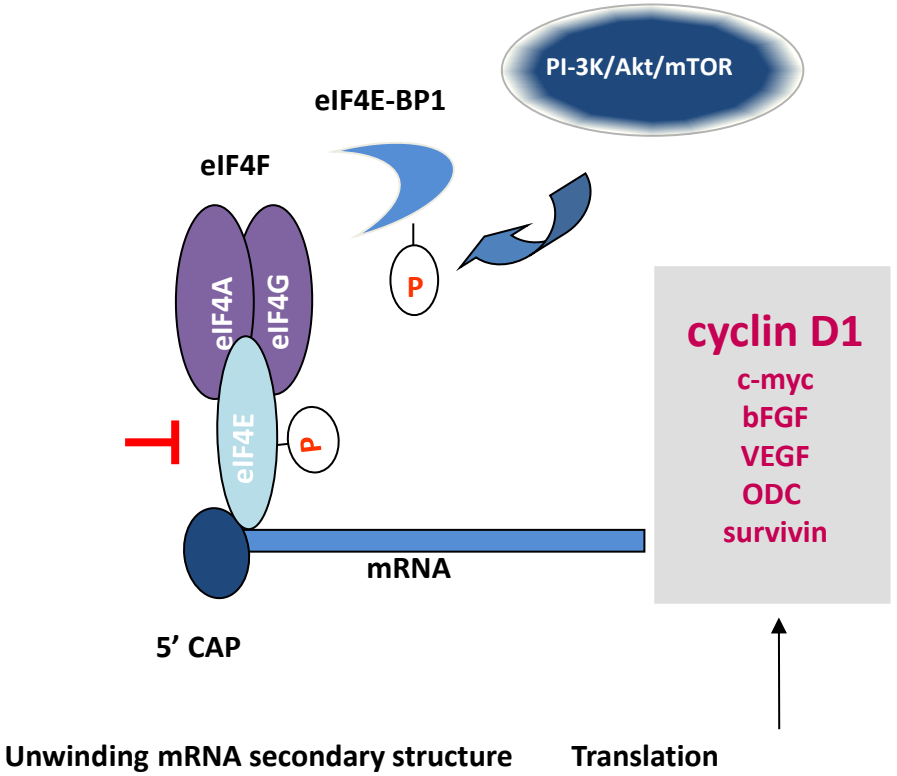
- Phase 1 stage targeted anticancer agent
  - Strong IP protection spanning to at least 2025
  - Novel target relevant to refractory cancers
    - Binds to eIF4E to inhibit translation of oncoproteins like cyclin D1

- 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: 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



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

ir@onconova.us