Corporate Update

June 2020

NASDAQ: ONTX

DISCLAIMER ON 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. This presentation assumes the Company raises capital for disclosed product development plans. 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.

OUR PRIORITIES

- **Announce topline INSPIRE survival data for IV rigosertib in 2H 2020**
  - **HR-MDS and VHR-MDS**
- **NDA preparation and commercialization readiness**
- **Explore rigosertib in additional RAS-mutated cancers**

Additional Pipeline Objectives

- Oral rigosertib + azacitidine in HMA-naïve HR-MDS patients
  - Initiate Phase 2/3 study
- Rigosertib + nivolumab in K-RAS mutated NSCLC
  - Initiate clinical studies
- ON 123300, a novel CDK 4/6 and ARK 5 Inhibitor
  - Submit IND to FDA for clinical development

RIGOSERTIB, MDS, & BEYOND

- **High unmet medical need in MDS**
  - No approved drugs after failure of standard of care
  - No HR-MDS new approvals in 15+ years
  - Promising survival signal at prospectively-planned 2018 interim analysis
  - Available for partnering in strategic territories

HR-MDS

INSPIRE Survival Data
Expected 2H20

1st-Line Combination Trial

Beyond HR-MDS

Lower-Risk MDS
KRAS+ NSCLC
Other KRAS+ Cancers
Rare Diseases (RASopathies)

ON 123300
CDK-Targeted NCE

MDS AND THE OPPORTUNITY

Malignant bone marrow disorder

- Acquired cytogenetic and genomic abnormalities
- Typically only in the marrow

US prevalence is 59,000

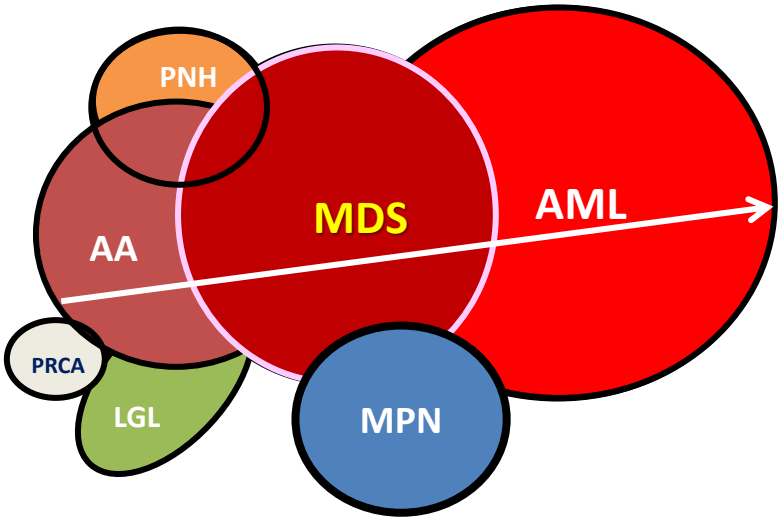
- 13,000 have higher risk (HR) MDS
- 10,000 2nd-line patients

Available treatments

- Limited to hypomethylating agents (HMAs)
- Vidaza (BMS) and Dacogen (Eisai/J&J)
- Approved 10+ years ago

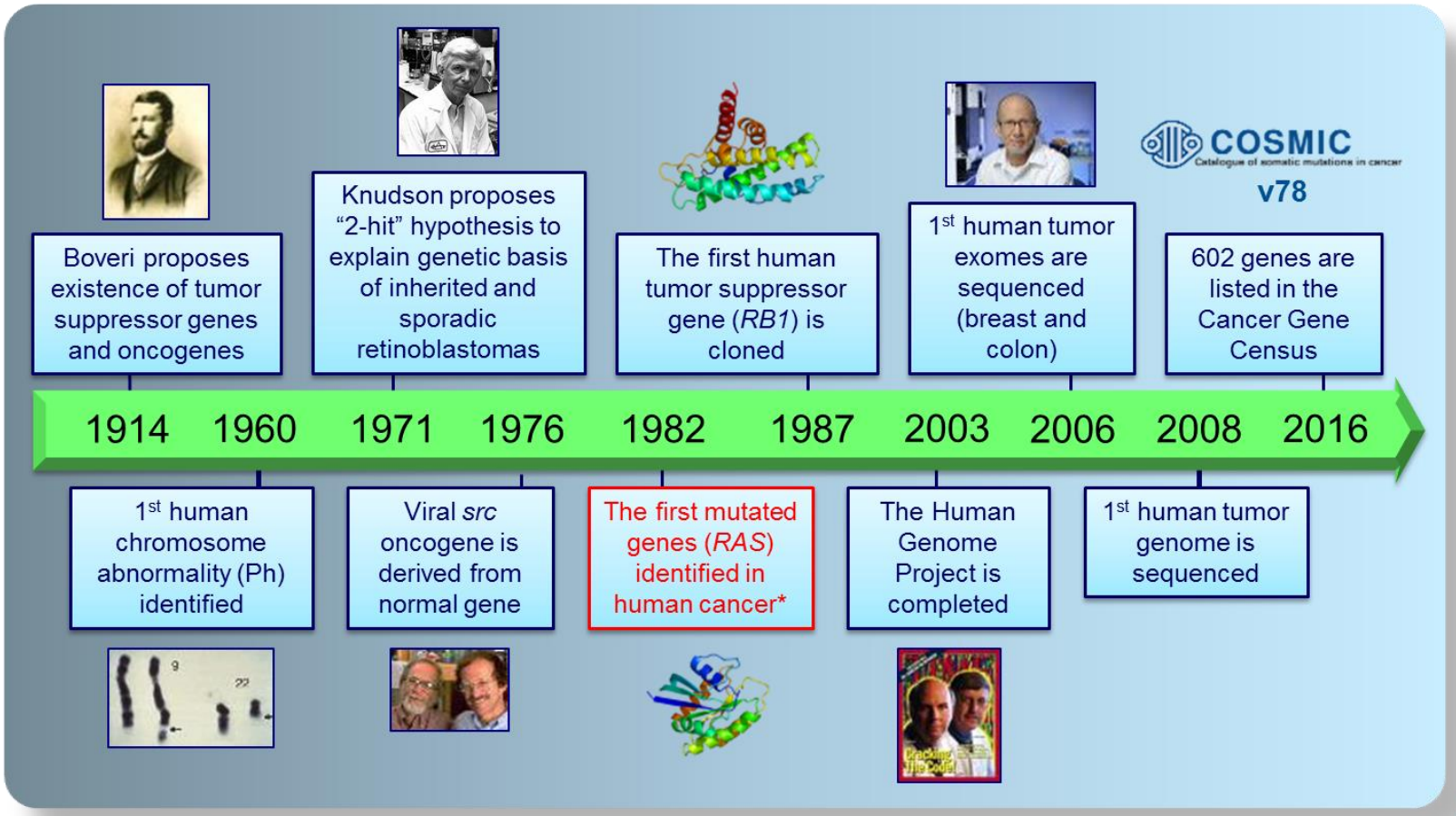
No approved therapy following HMA failure

- $Billions opportunity



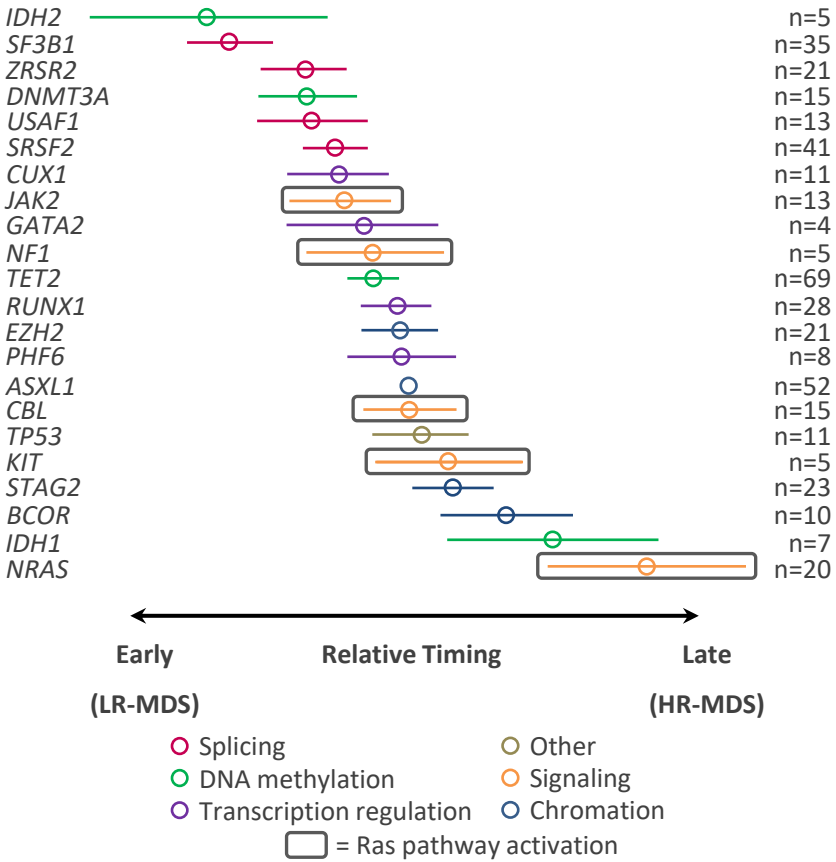
RAS MUTATIONS IN CANCER

HRAS, KRAS and NRAS comprise the most frequently mutated oncogene family (~25%)

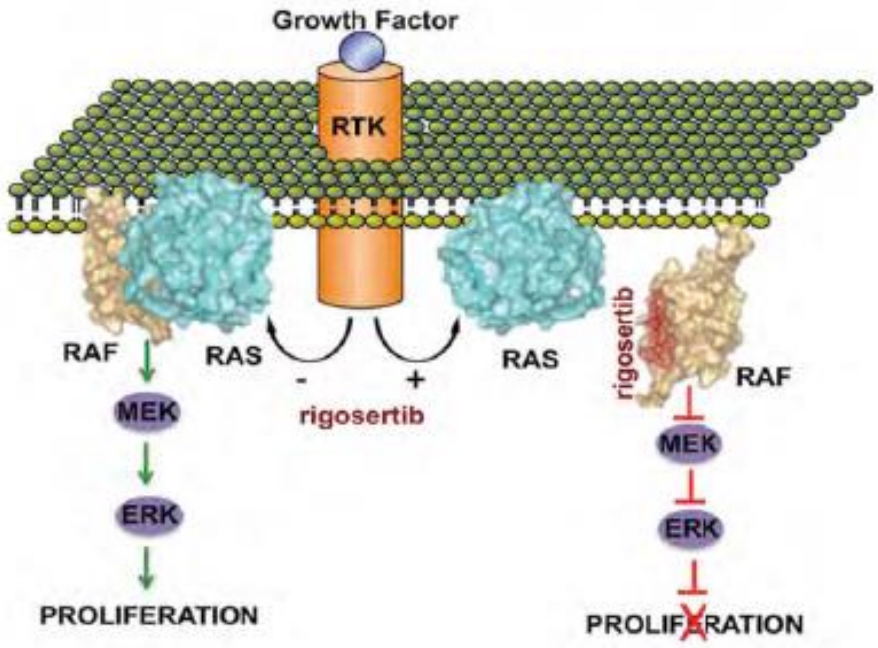


MDS AND THE MOA OF RIGOSERTIB

Temporal Order of Gene Mutations in 107 MDS Patients*



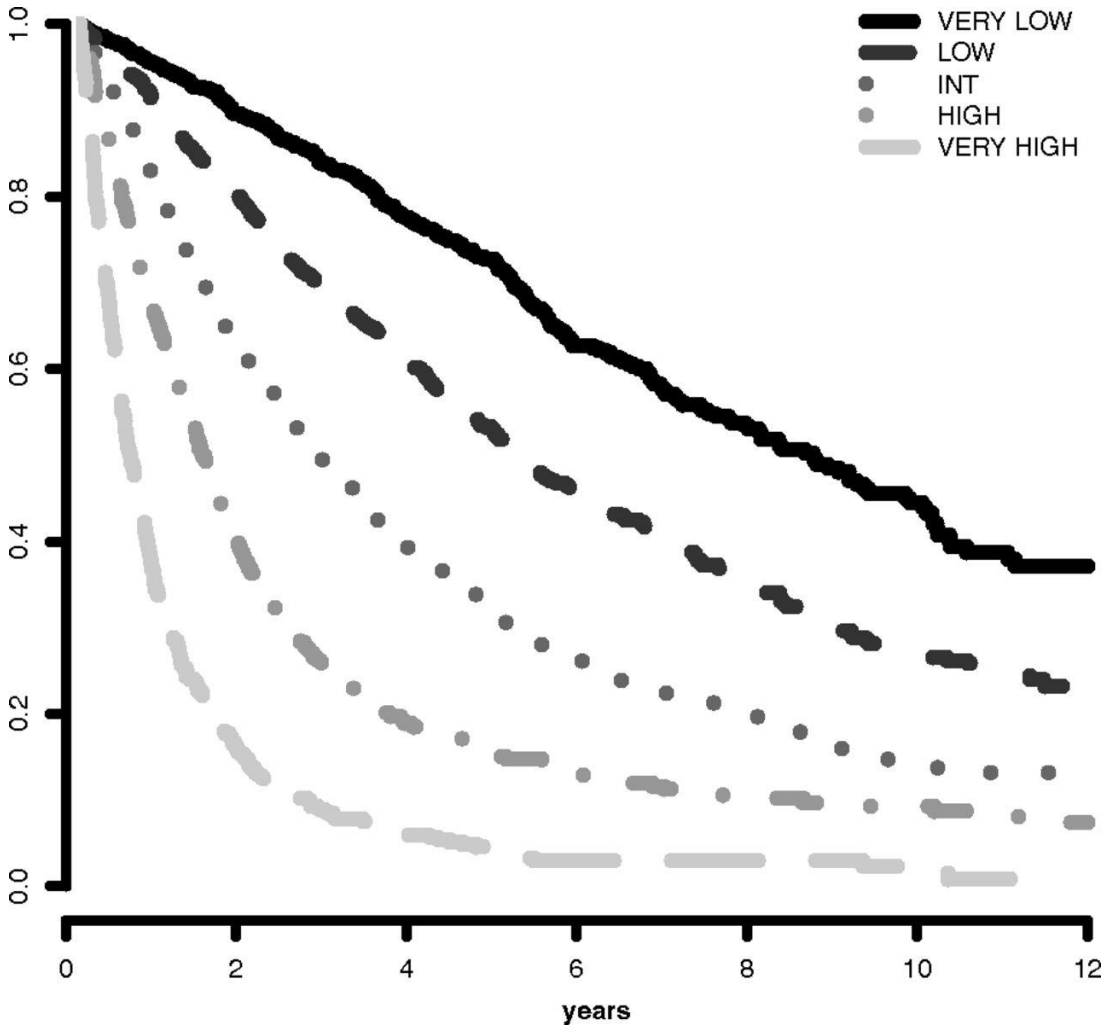
RAS targeted novel mode of action**



* Adapted from Papaemmanuil et al., 2013 Blood

** Athuluri-Divakar SK, Cell 2016;165:643

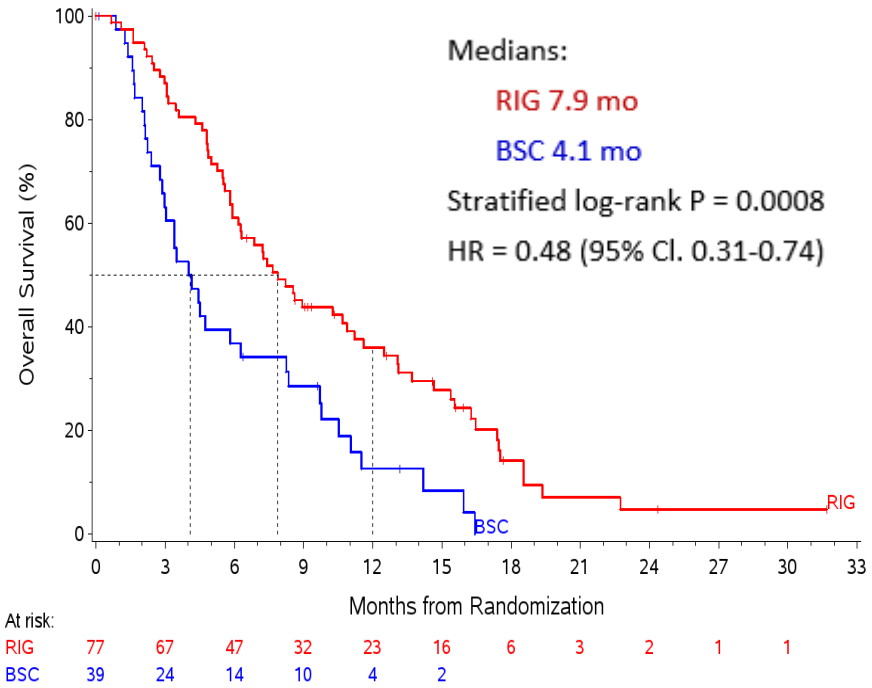
REVISED IPSS



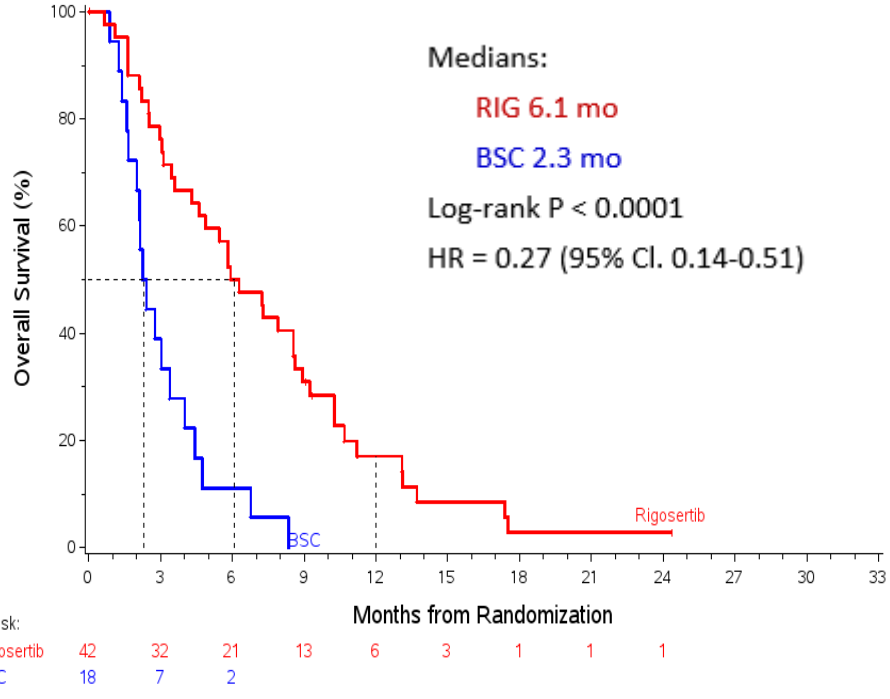
Greenberg et al. Blood 2012;120:2454-65

PROPOSED PATIENT POPULATION FOR INSPIRE

Entire ITT population

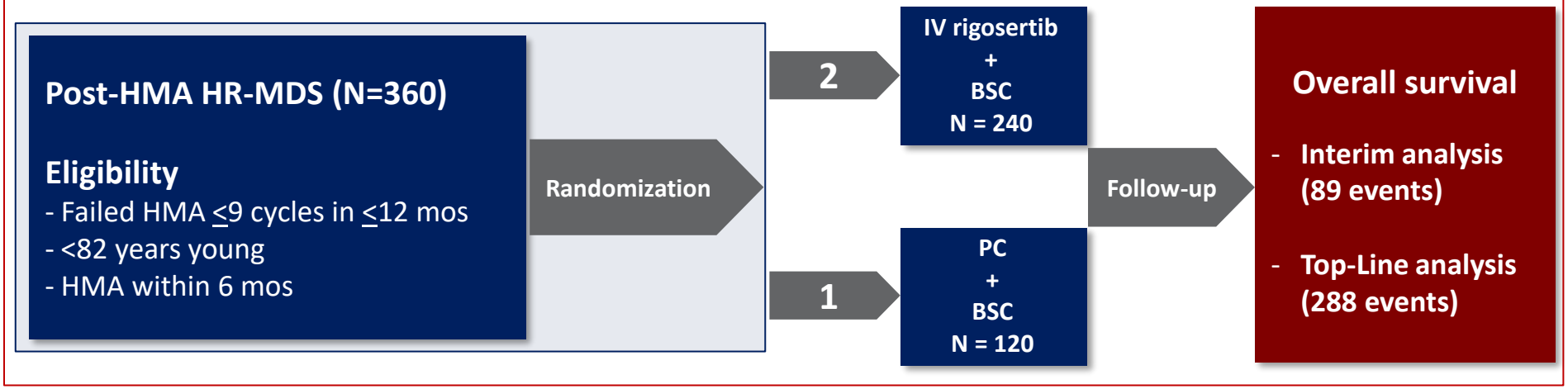


Very High Risk (VHR) population



- Age < 82 years
- Duration of prior HMA ≤ 9 cycles of prior HMA in ≤ 12 months
- Time from last dose of prior HMA to random assignment ≤ 6 months

INSPIRE DESIGN AND OBJECTIVES



- **Stratification at randomization**
  - **VHR vs. non-VHR**
  - **US vs. Europe vs. Asia**
- **Post Interim Analysis**
  - **Promising Survival Signal Seen**
  - **ITT population**
    - **α = 0.04**
    - **Power = 0.80**
    - **Target HR $\leq$ 0.72**
    - **Reduce mortality by ≥ 28%**
  - **VHR subgroup**
    - **α = 0.01**
    - **Power = 0.80**
    - **Target HR $\leq$ 0.55**
    - **Reduce mortality by ≥ 45%**

INSPIRE UPDATE & OBSERVATIONS

Status

- Completed enrollment in March 2020
- 85% of the required 288 events exceeded as of March 2020

High proportion of VHR subgroup may have favorable implications

- >70% seen at interim analysis on INSPIRE
- Validates the trial design and strict patient eligibility criteria
  - *failure to respond or progress within 9 cycles of AZA*

Innovative features of study design

- Deep genomic sequencing at study entry and at key time points
- Interim analysis showed promising survival signal for rigosertib arm
- Two opportunities for approval
  - First analysis of survival in the ITT Population
  - Sequential analysis of the VHR Population, if necessary

Directed at unmet medical need in MDS

- No approved drug in this space following HMA failure
- Orphan drug designation in US and EU

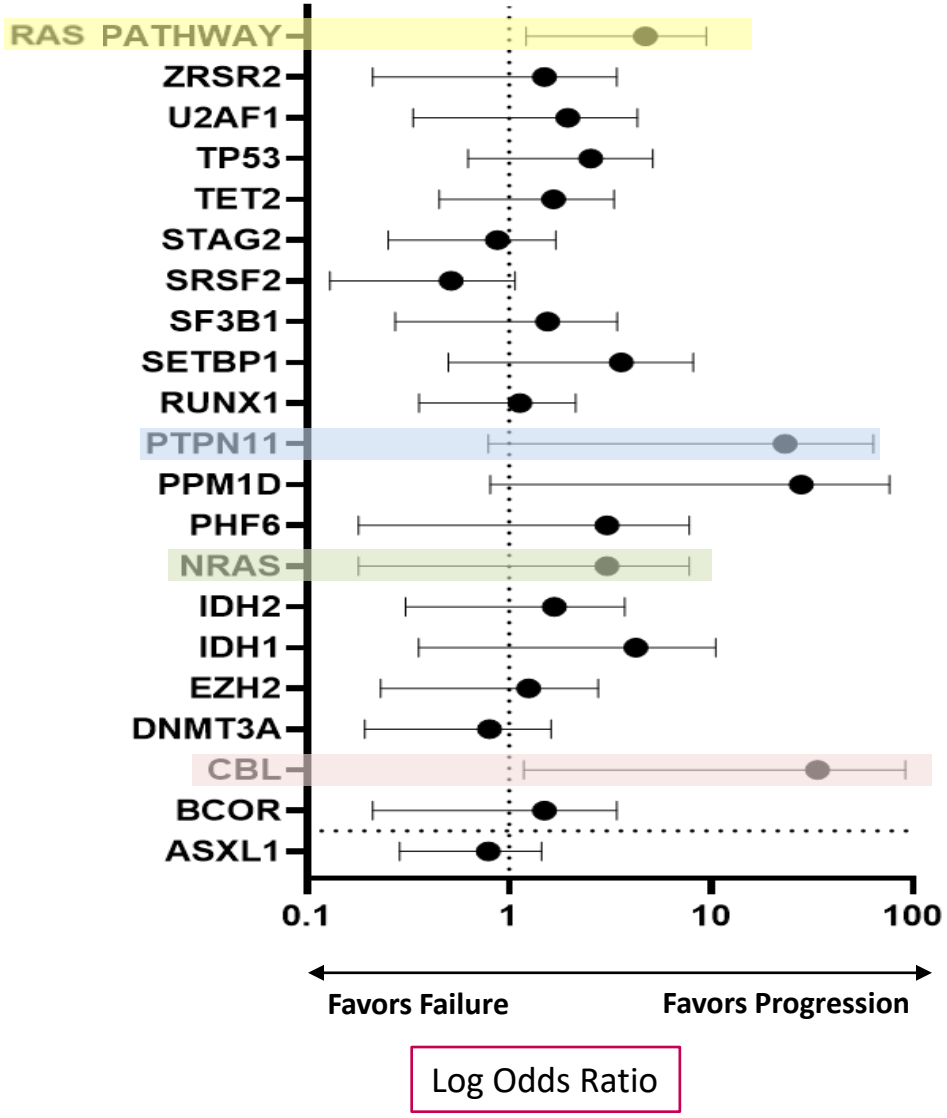
ONCONOVA THERAPEUTICS

Genomic Profiling in Patients with Higher Risk Myelodysplastic Syndrome (HR MDS) Following HMA Failure: Baseline Results from the Inspire Study (04-30)

Guillermo Garcia-Manero, MD[1], Anna Jonasova, MD, PhD[2], Selina M. Luger, MD, FRCPC[3], Aref Al-Kali, MD[4], David Valcárcel, MD[5], Erica D. Warlick, MD[6], Wieslaw W. Jedrzejczak, MD, PhD[7], María Díez-Campelo, MD, PhD[8], Patrick S. Zbyszewski, MBA[9], Christopher Cavanaugh[9], Richard C. Woodman, MD[9], Steven M. Fruchtman, MD[9] & Koichi Takahashi, MD[10]

[1]University of Texas MD Anderson Cancer Center, Department of Leukemia, Houston, TX; [2]1st Medical Department - Hematology, General Hospital, Prague, Czech Republic; [3]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [4]Division of Hematology, Mayo Clinic, Rochester, MN; [5]Planta Baixa, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [6]Division of Hematology, Oncology and Transplantation, University of Minnesota, Minneapolis, MN; [7]MTZ Clinical Research, Medical University of Warsaw, Warsaw, Poland; [8]Hematology Department, Institute of Biomedical Research of Salamanca, University Hospital of Salamanca, Salamanca, Spain; [9]Onconova Therapeutics, Inc., Newtown, PA; [10]Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

MUTATIONAL RESULTS ACCORDING TO DISEASE PROGRESSION OR HMA FAILURE AT TIME OF STUDY ENTRY



*RAS PATHWAY includes NRAS, KRAS, CBL, PTPN11, and NF1

Mutations identified in ≥ 4 patients are listed individually

N=159

- ***136 enrolled***
- ***23 screen failures***

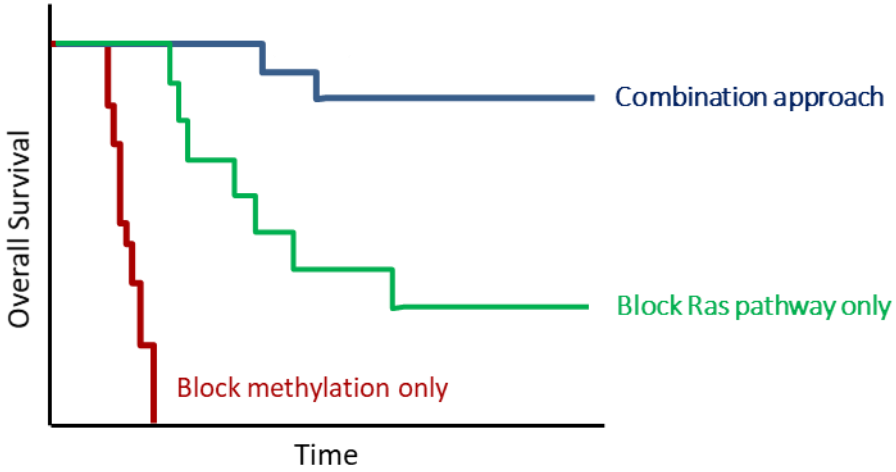
ORAL RIGOSERTIB DEVELOPMENT PROGRAM

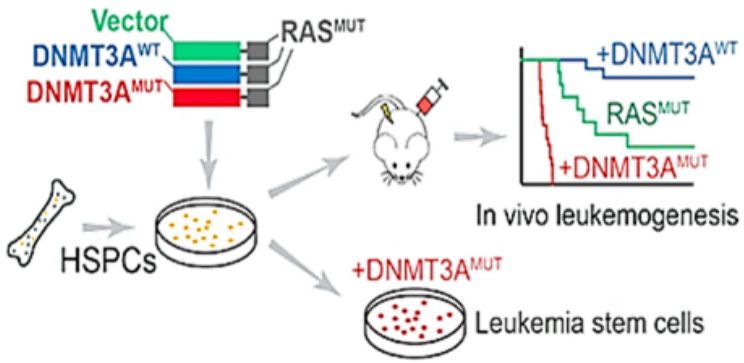
COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

Preclinical evidence supports synergy of rigosertib + azacitidine

AML Mouse Model

Validation of combination approach

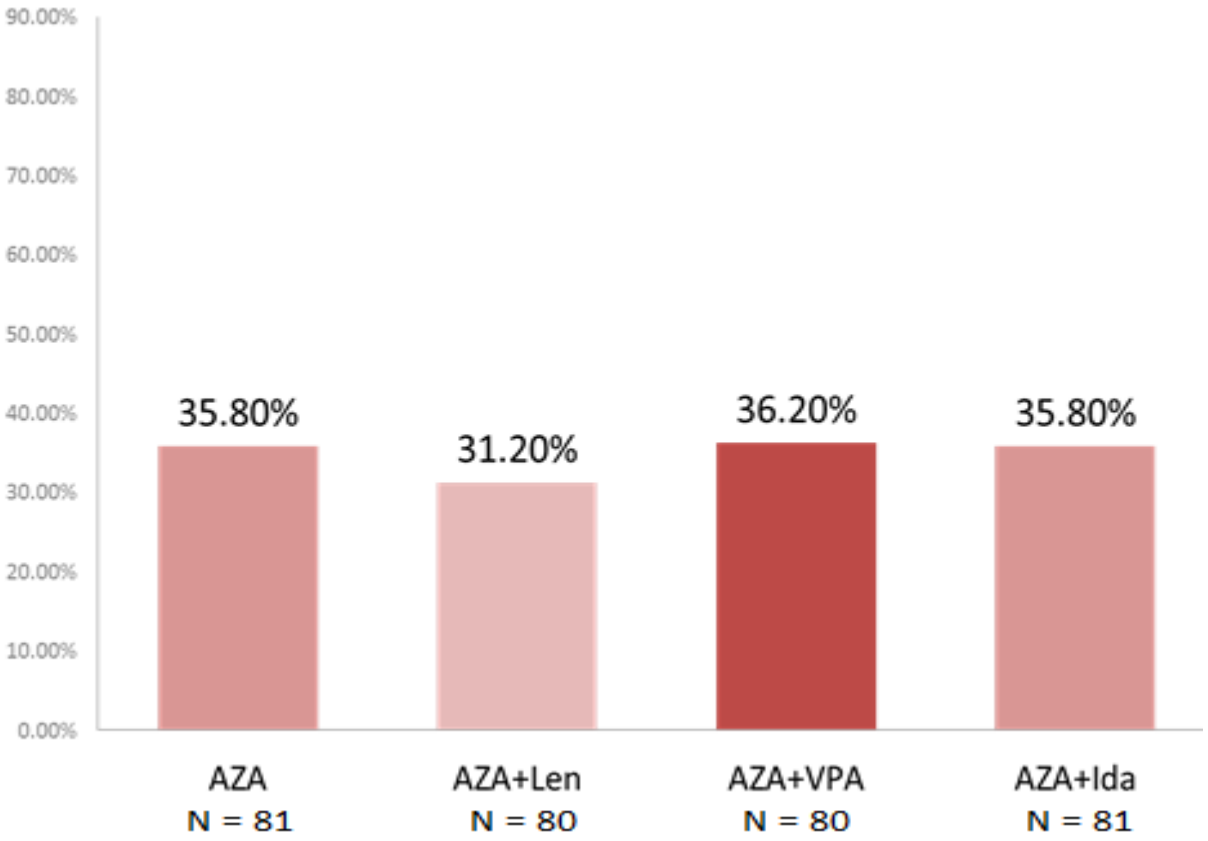




Lu et al., 2016 Cancer Cell

ORAL RIGOSERTIB + STANDARD DOSE AZACITIDINE DOUBLET RESPONSE RATES: (CR/PR/MCR)

PATIENTS RECEIVED A MEDIAN OF 7 CYCLES



Lionel Adès et al: ASH; 2018

ORAL RIGOSERTIB + STANDARD DOSE AZACITIDINE DOUBLET RESPONSE RATES: (CR/PR/MCR)

PATIENTS RECEIVED A MEDIAN OF 7 CYCLES

** Navada et al: ASH; 2018 Median Duration of Treatment is 7.8 months (0.7-25.1)

Note: these are not head-to-head studies from which inferences or comparisons can be drawn, but rather serve as part of the basis for company's further investigation

Lionel Adès et al: ASH; 2018

TREATMENT-EXPERIENCED, HMA-NAÏVE ≥ 840MG/DAY

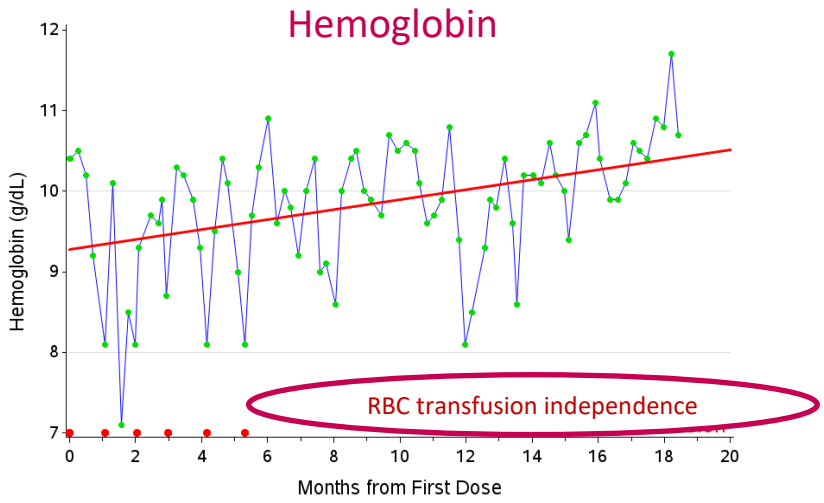
Evaluable for response	29*
Overall response per IWG 2006	26 (90%)
CR+PR	10 (34%)
Complete remission (CR)	10 (34%)
Partial remission (PR)	0
Marrow CR + Hematologic Improvement	5 (17%)
Hematologic Improvement alone	3 (10%)
Marrow CR alone	8 (28%)
Stable disease	3 (10%)
Progression	0
Median duration of response (months)	12.2 (range, 0.1-24.2+)
Median duration of treatment (months)	7.8 (range, 0.7-25.1+)
Median time to initial/best response (cycles)	1/4

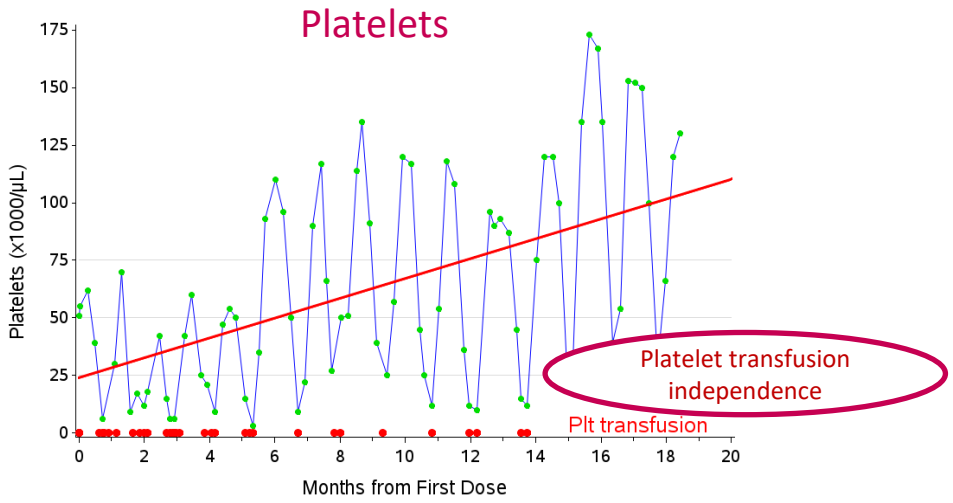
**** Includes 2 patients previously treated with non-HMA chemotherapy***

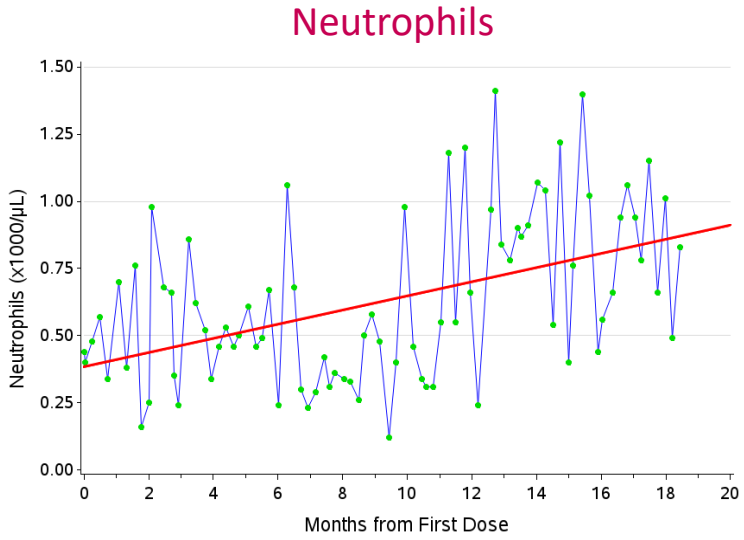
Navada et al ASH 2019

AZA + RIGO MAY LEAD TO TRANSFUSION INDEPENDENCE

Single patient case data:*







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

** Individual patient response data may vary*

RIGOSERTIB COMBINATION THERAPY NEXT STEPS

Step	Status	Remarks
Phase 2 expansion *Fully enrolled*	Completed	▪ Dose and schedule of ≥ 840 mg daily dose updated and presented at ASH 2019
Phase 2/3 randomized study with azacitidine control arm	Initiate in Conjunction with INSPIRE Readout	▪ Initial FDA feedback obtained ▪ Phase 2/3 protocol to be submitted ▪ Rapid enrollment expected ▪ Primary endpoint is response, thus may be achieved in <6-9 months after patient is enrolled

EXPANDED STUDIES & INDICATIONS FOR RIGOSERTIB

EFFECT OF RIGOSERTIB ON PATIENT-DERIVED XENOGRAFTS

Metastatic lung adenocarcinoma

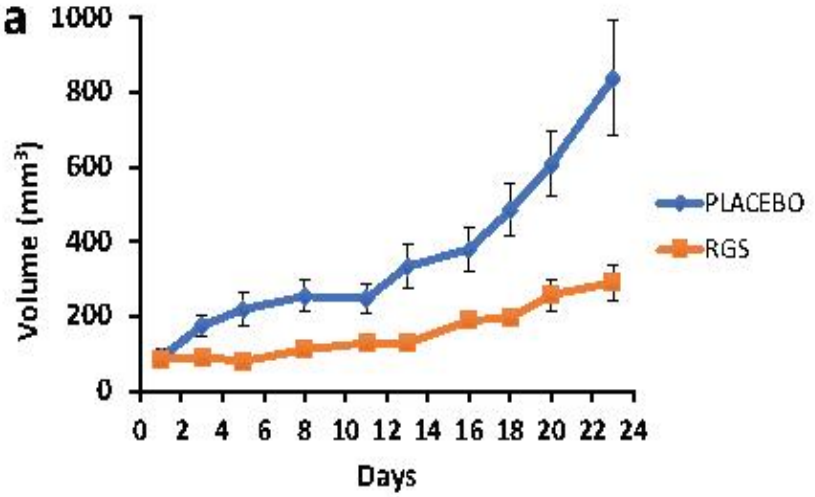
AJCC IV

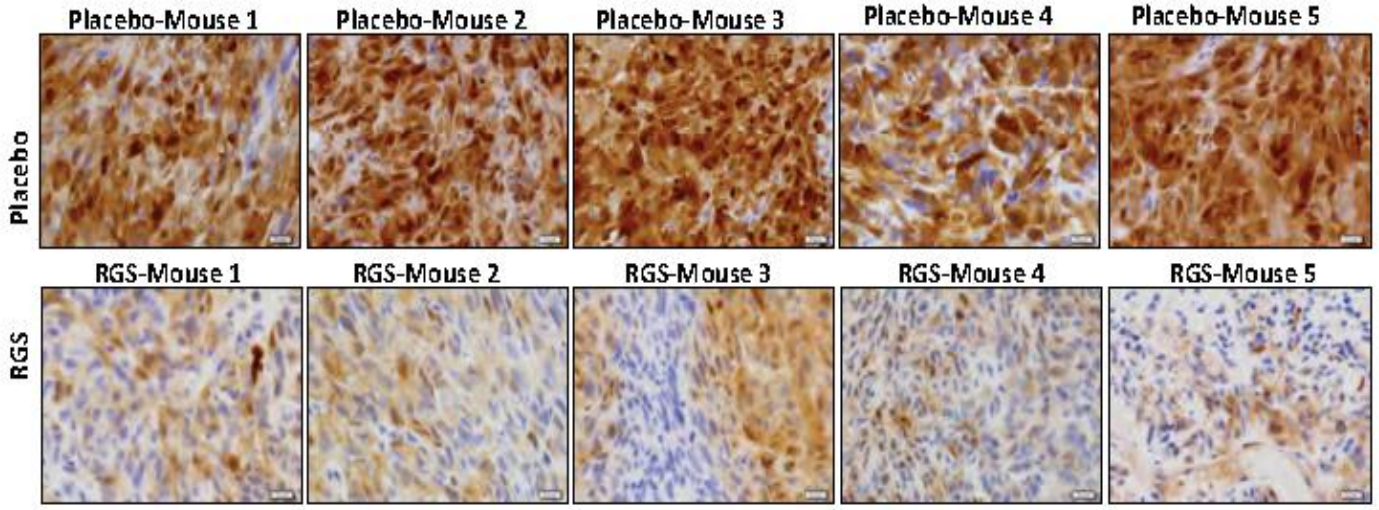
53 y/o female

***KRAS*^{G12D}**

ALK+

89.1% PD-L1+ (surface)





pERK Staining

PHASE 1 STUDY OF RIGOSERTIB + PD-1 IN ADVANCED NSCLC

PI: Dr. Raj Veluswamy, MSSM

Rigosertib + Nivolumab in Stage IV Lung Adenocarcinoma Patients with KRAS Mutation who Progressed on First-Line Treatment

Main Inclusion Criteria

1. Metastatic lung adenocarcinoma with KRAS mutation
2. Progressed on SOC 1st-line
3. ≥ 18 years old with ECOG PS 0-2

Dosage and Administration: 28-Day Cycles

Rigosertib – Oral (days 1 – 21):
- Dose 1: 280mg twice daily
- Dose 2: 560mg in am, 280mg in pm
- Dose 3: 560mg twice daily

Nivolumab - IV; days 1 and 14 at 240 mg Q 2 weeks

Dose Escalation Phase (8-18 Patients)

Accelerated Titration Design (ATD):

Single patient cohorts until:
- D3 tolerated → expand to 6 patient cohort to establish MTD
- Grade 2 toxicity → ATD ends; 3+3 Design starts using DLT
- Primary Objective: MTD/RPTD (≤1 out of 6 patients experiences DLT)

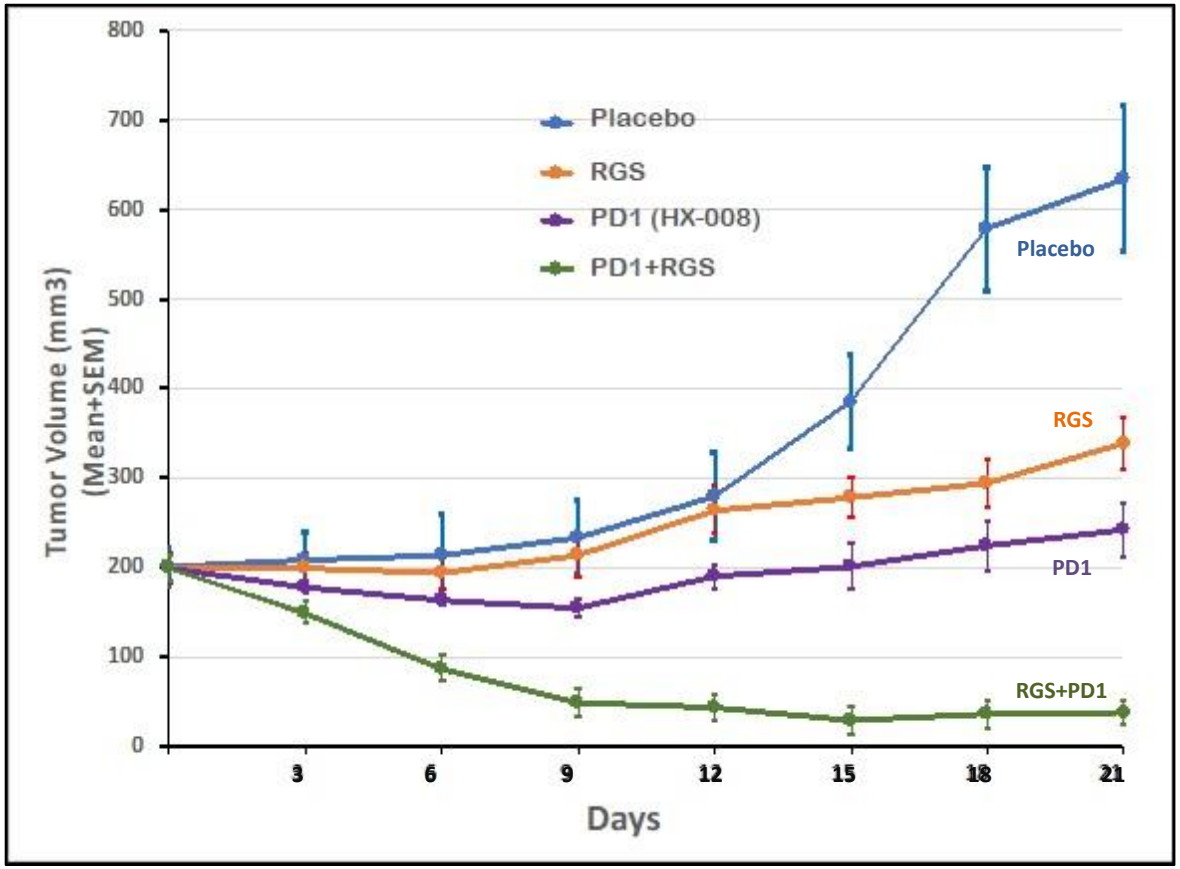
Expansion Phase

12 patients at MTD of Rigosertib with Nivolumab × 6 cycles

Secondary objectives
- Confirm safety and tolerability of MTD
- Evaluate efficacy through ORR
- Assess PFS and OS

RIGOSERTIB + PD-1 ARE SYNERGISTIC IN A PRE-CLINICAL KRAS+ COLORECTAL CANCER MODEL

MC30 Colorectal Cancer (CRC) Tumor Model

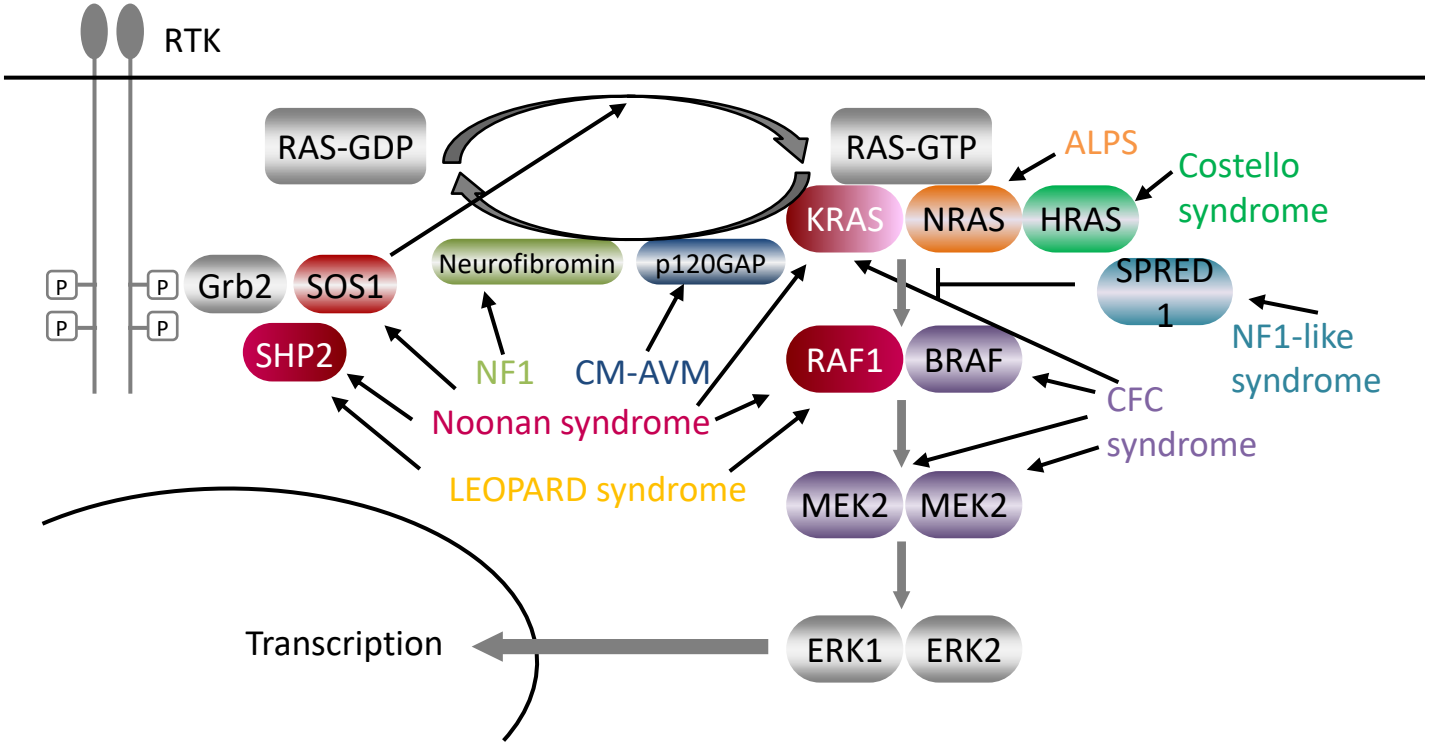


DATA BY HANX BIOPHARMACEUTICALS

RASOPATHIES: RIGOSERTIB FOR RARE PEDIATRIC CANCERS

Milestones: Goal is a pediatric voucher

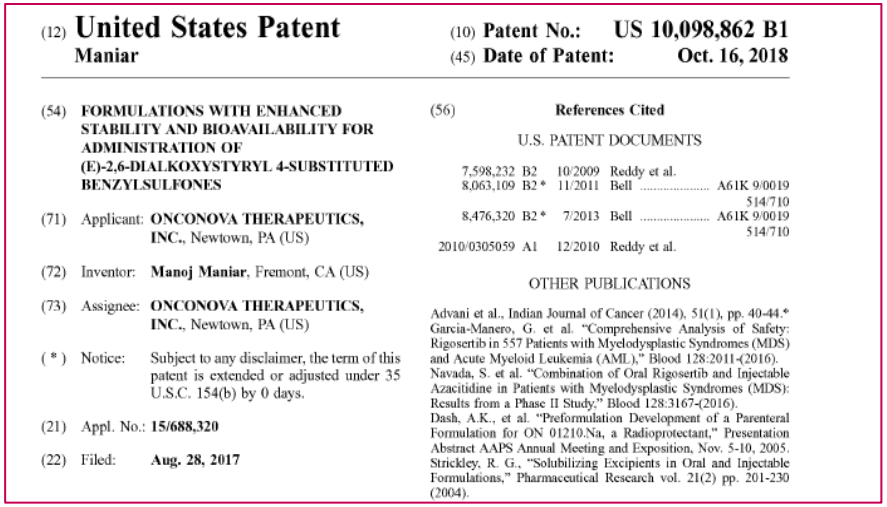
- NCI CRADA signed January 2018
- UCSF non-clinical program initiated
  - Funded by LLS
- JMML clinical program anticipated



EXPANDING AND EXTENDING RIGOSERTIB PATENT COVERAGE

- Strong existing patent estate
  - Existing coverage of composition of matter (e.g. U.S. 7,598,232), formulations, combinations and methods in US and many countries worldwide
- Supplemented by Orphan Designation for MDS in US and Europe
- US patent 10,098,862 extends IP runway to 2037

- US Patent 10,098,862
  - Pending in PCT and non-PCT countries worldwide
  - Covers injectable and oral products



(12) **United States Patent**
Maniar

(10) **Patent No.: US 10,098,862 B1**
(45) **Date of Patent: Oct. 16, 2018**

(54) **FORMULATIONS WITH ENHANCED STABILITY AND BIOAVAILABILITY FOR ADMINISTRATION OF (E)-2,6-DIALKOXYSTYRYL 4-SUBSTITUTED BENZYLSULFONES**

(71) Applicant: **ONCONOVA THERAPEUTICS, INC.**, Newtown, PA (US)

(72) Inventor: **Manoj Maniar**, Fremont, CA (US)

(73) Assignee: **ONCONOVA THERAPEUTICS, INC.**, Newtown, PA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/688,320**

(22) Filed: **Aug. 28, 2017**

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,598,232	B2	10/2009	Reddy et al.	
8,063,109	B2 *	11/2011	Bell	A61K 9/0019 514/710
8,476,320	B2 *	7/2013	Bell	A61K 9/0019 514/710
2010/0305059	A1	12/2010	Reddy et al.	

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Advani et al., Indian Journal of Cancer (2014), 51(1), pp. 40-44.*
Garcia-Manero, G. et al. "Comprehensive Analysis of Safety: Rigosertib in 557 Patients with Myelodysplastic Syndromes (MDS) and Acute Myeloid Leukemia (AML)," Blood 128:2011-(2016).
Navada, S. et al. "Combination of Oral Rigosertib and Injectable Azacitidine in Patients with Myelodysplastic Syndromes (MDS): Results from a Phase II Study," Blood 128:3167-(2016).
Dash, A.K., et al. "Preformulation Development of a Parenteral Formulation for ON 01210.Na, a Radioprotectant," Presentation Abstract AAPS Annual Meeting and Exposition, Nov. 5-10, 2005.
Strickley, R. G., "Solubilizing Excipients in Oral and Injectable Formulations," Pharmaceutical Research vol. 21(2) pp. 201-230 (2004).

ON 123300: NEXT-GENERATION CDK4/6 INHIBITOR

Also targets ARK5 (NUAK1)

Differentiation for a Competitive Field

- Ibrance®, Kisqualí® and Verzenio®
  - Hailed as breakthroughs in cancer therapy
  - First FDA approval for CDK 4/6 inhibitor is for breast cancer
- ON 123300 differentiated features
  - Also targets ARK5 controlling cellular metabolism and survival
  - Potential to act as single agent
  - May be active in resistant cells

HanX Biopharmaceuticals Partnership

- Specialty oncology company
  - Funding IND-enabling studies
  - License for Greater China
  - Onconova retains ROW rights
- Upfront payment, milestones, royalties
- Phase 1 stage PD-1 checkpoint antibody
- Checkpoint blockade + CDK inhibition believed to be synergistic
- Awaiting required manufacturing data
- US IND submission anticipated 4Q 2020
- China IND approved January 2020

PARTNERING ROSTER AND OPPORTUNITIES BY REGION

Rigosertib – a differentiated orphan drug, patent-protected RAS mimetic

Rigosertib by Region	Partnering Availability
Europe	Available for Partnering
China and Asia (ex. Japan and Korea)	Available for Partnering
Japan & Korea (2011)	SymBio Pharmaceuticals Limited
Latin America (2018)	PINT PHARMA
Canada (2019)	Knight
Australia & New Zealand (2019)	Specialised Therapeutics®
Rest of World (i.e. MENA)	Available for Partnering

PARTNERING OPPORTUNITIES FOR PIPELINE PRODUCTS

- **ON123300 - Novel CDK 4/6 and and ARK5 Inhibitor**
  - Commercially available CDK 4/6 inhibitors are multi billion franchises - abemaciclib (Verzenio), palbociclib (Ibrance) and ribociclib (Kisqali)
  - US IND Expected in Q4 2020
  - Phase 1 Study in China in 2H 2020

ON123300 by Region	Partnering Availability
Rest of World (ex. China)	Available for Partnering
China	HanX Biopharmaceuticals

- **Briciclib - Novel Phase 1 eIF4E Inhibitor**
  - Effector Therapeutics / Pfizer and Takeda / Millennium in phase 1/2 clinical development with compounds related to the eIF4E pathway

Briciclib by Region	Partnering Availability
World	Available for Partnering

CAPITALIZATION & CASH

Outstanding Securities	As of 3/31/2020
Common Stock Outstanding *(5/1/20)*	167,416,070
Options Outstanding (WAEP: $25.22)	1,017,393
Warrants (WAEP: $0.95) *Over 80% in-the-money as of 5/13/20*	28,751,412
Cash Balance*	$31.0 Million

* Sufficient cash to fund ongoing trials and operations into 3Q 2021

MANAGEMENT TEAM

	Steven M. Fruchtman, M.D. *President & CEO*	Mount Sinai, Novartis, Janssen, Syndax, Allos Therapeutics, Spectrum Pharmaceuticals
	Richard Woodman, M.D. *Chief Medical Officer*	University of Calgary, Scripps Clinic & Research Institute, Novartis, Ortho Biotech Products
	Mark Guerin *Chief Financial Officer*	Barrier Therapeutics, Cardiokine, Pricewaterhouse Coopers
	Manoj Maniar, Ph.D. *Sr., VP, Product Development*	Alcon, SRI
	Avi Oler, JD, MBA *Head of Corporate Development and General Counsel*	Spectrum Pharmaceuticals, Kirkland & Ellis, Center for Financial Research & Analysis, Lehman Brothers


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THERAPEUTICS
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