Issuer Free Writing Prospectus dated September 13, 2019
Filed Pursuant to Rule 433
Relating to the Preliminary Prospectus Supplement dated September 13, 2019
Registration Statement No. 333-221684

DISCLAIMERS

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.

Free Writing Prospectus Statement

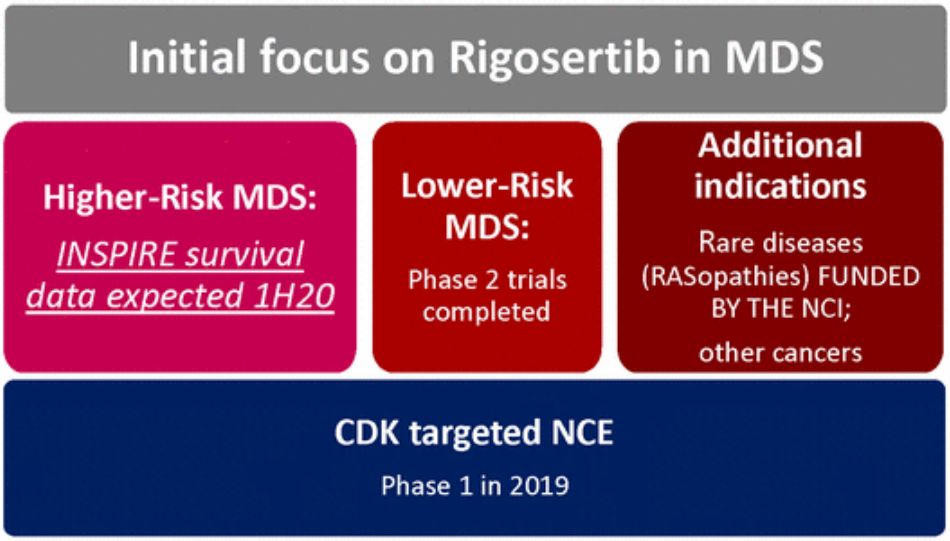
This presentation highlights basic information about us and the proposed offering. Because it is a summary, it does not contain all of the information that you should consider before investing. We have filed a registration statement (including a preliminary prospectus supplement) with the SEC for the offering to which this presentation relates. Before you invest, you should read the preliminary prospectus supplement in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering.

You may access these documents for free by visiting EDGAR on the SEC Web site at http://www.sec.gov. The preliminary prospectus supplement, filed on September 13, 2019 is available on the SEC Web site at http://www.sec.gov. Alternatively, we or any underwriter participating in the offering will arrange to send you the prospectus if you contact Think Equity, a division of Fordham Financial Management, Inc., Prospectus Department, 17 State Street, 22nd Floor, New York, New York 10004, telephone: (877) 436-3673 or e-mail: prospectus@think-equity.com.

This presentation does not constitute an offer to sell, or the solicitation of an offer to buy, nor will there be any sale of these securities in any state or other jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such state or jurisdiction. The offering will only be made by means of a prospectus pursuant to a registration statement that is filed with the SEC after such registration statement becomes effective.

ONCONOVA THERAPEUTICS, INC.

- Onconova Therapeutics, Inc. is a Phase 3 stage biopharmaceutical company focused on discovering and developing novel small molecule drug candidates to treat cancer.
- Upcoming Phase 3 top-line data in Higher-Risk Myelodysplastic Syndromes (HR-MDS)
  - Promising survival signal at prospectively planned Interim Analysis
  - Rigosertib partnered in Japan / Korea, Latin America, and China
  - Additional partnerships anticipated in available territories



MANAGEMENT FOCUS

Priorities

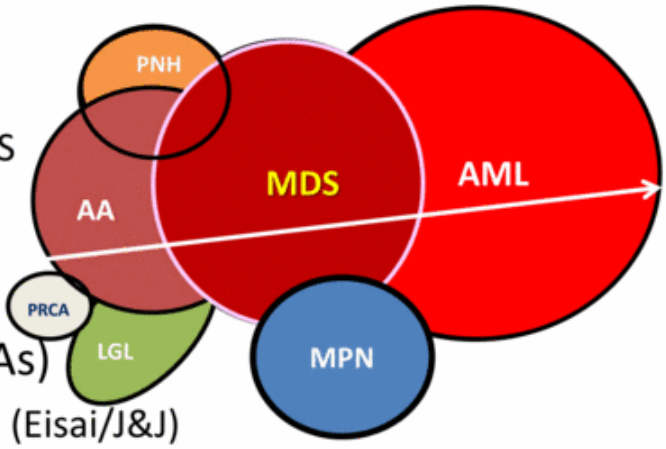
- **Complete INSPIRE accrual and obtain pivotal survival data 1H20**
- **Complete business development transactions**

Other Goals

- Finalize SPA agreement with FDA for combination pivotal trial
  - Seeking Collaboration to Initiate Future Pivotal Ph 3 Trial
- Complete Rasopathy PDX and pre-clinical models and initiate a Phase 1 clinical trial in Ras driven pediatric cancer
- Support initiation of rigosertib doublet study in KRAS + NSCLC
- Submit IND to FDA for ON 123300 (Novel CDK 4/6 and ARK 5 Inhibitor)

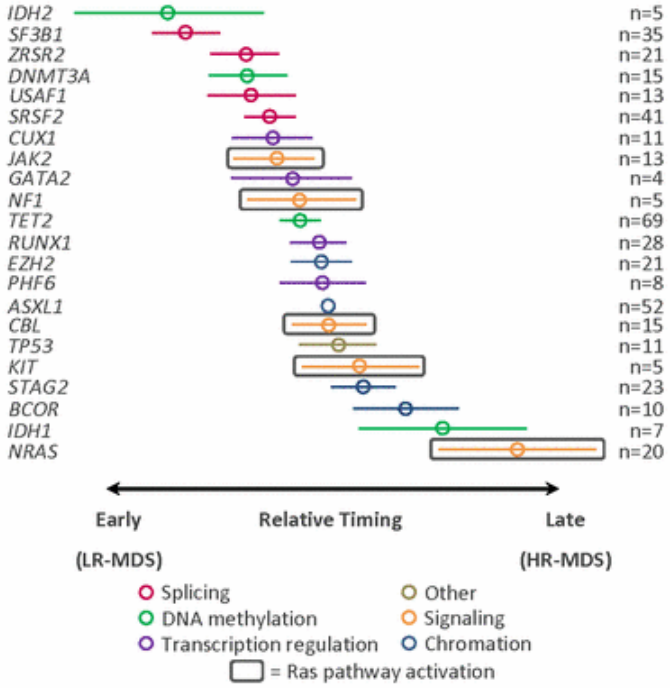
MDS IS RELATED TO OTHER BONE MARROW DISEASES
WHAT EXACTLY IS MDS?

- MDS: malignant bone marrow disorder characterized by:
  - Acquired cytogenetic and genomic abnormalities, but typically only in the marrow
- US prevalence is 59,000
  - ~13,000 have higher risk (HR) MDS
  - ~10,000 second-line patients
- Available Treatments limited to hypomethylating agents (HMAs)
  - HMAs: Vidaza (Celgene); Dacogen (Eisai/J&J)
  - Approved >decade ago; now off-patent
  - No approved therapy following HMA failure

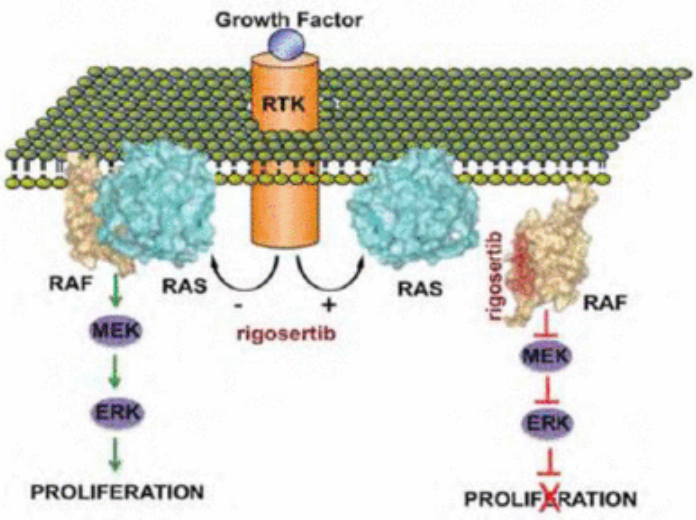


ABOUT MDS AND MOA OF RIGOSERTIB

Temporal Order of Gene Mutations in 107 MDS Patients*

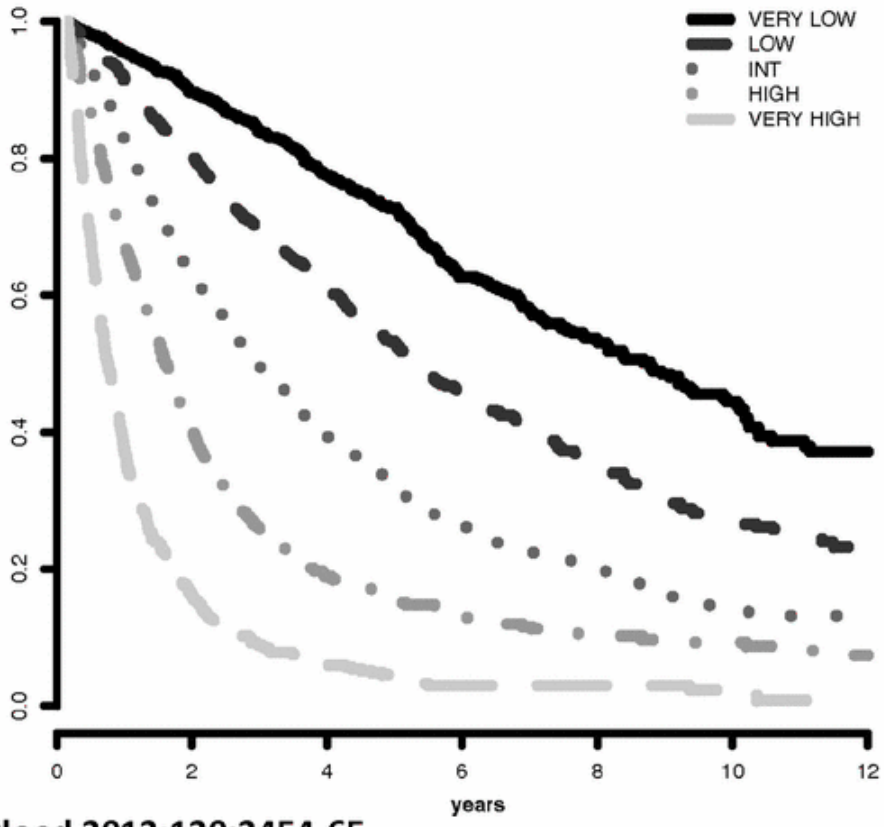


RAS targeted novel mode of action**



*Adapted from Papaemmanuil et al., 2013 Blood
**Athuluri-Divakar SK, Cell 2016;165:643

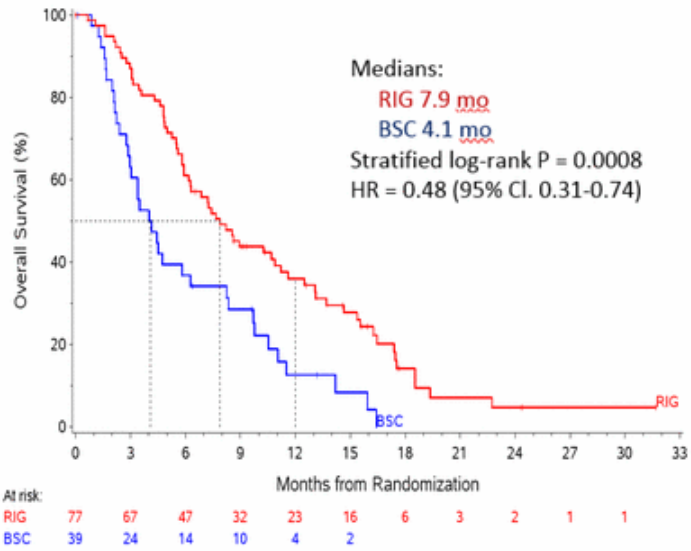
REVISED IPSS



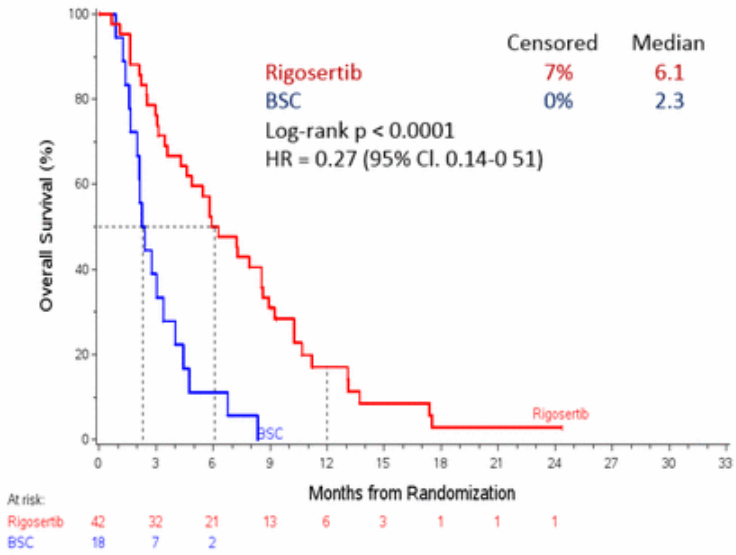
Greenberg et al. Blood 2012;120:2454-65

STUDY 04-21 : PROPOSED PATIENT POPULATION FOR INSPIRE

Entire ITT population

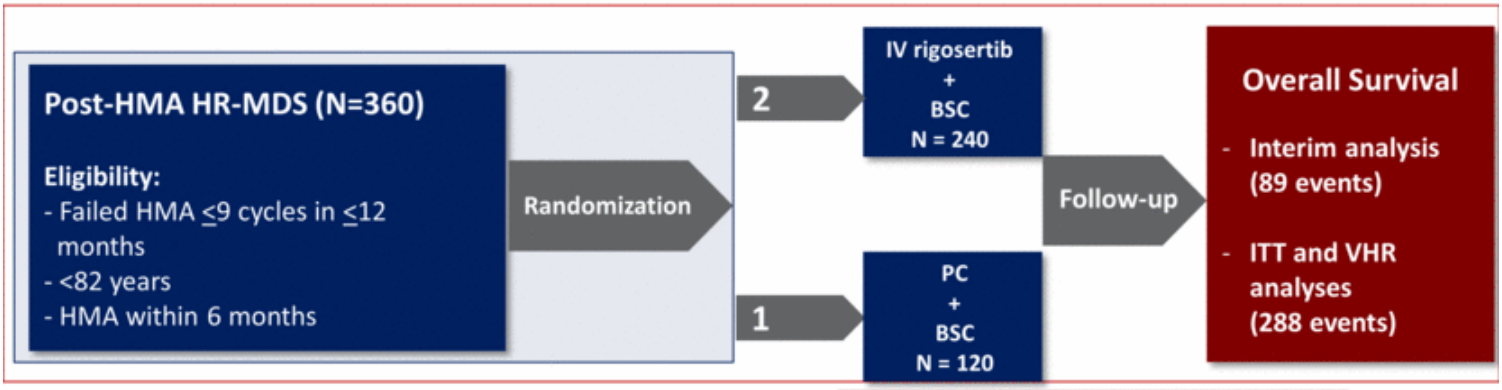


Very High Risk (VHR) population



- 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 STUDY DESIGN AND STATISTICAL OBJECTIVES



Innovative features of INSPIRE study design

- **Interim Analysis (January 2018) showed promising survival signal for rigosertib arm**
- **Genomic profiling at study entry and at key time points**

- **Stratification at randomization**
  - **VHR vs. non-VHR**
  - **U.S. vs. EUROPE vs. Asia**
- **Post Interim Analysis**
  - **ITT population**
    - **$\alpha = 0.04$**
    - **Power = 0.80**
    - **Target HR ≤ 0.72**
    - **Reduce mortality by ≥ 28%**
  - **VHR subgroup**
    - **$\alpha = 0.01$**
    - **Power = 0.80**
    - **Target HR ≤ 0.55**
    - **Reduce mortality by ≥ 45%**

INSPIRE: TIMELINES & OBSERVATIONS

- High proportion of VHR subgroup on current INSPIRE Trial 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*
  - VHR subgroup had significant OS advantage on ONTIME
- Median overall survival of INSPIRE
  - Control group survival could be <4 months due to higher VHR population
  - OS on control arm should not change; no new options to consider
  - May hasten timeline to pivotal data for requirement of 288 events
- INSPIRE directed to the unmet medical need in MDS
  - No approved drug in this space
  - Orphan drug designation in US and EU

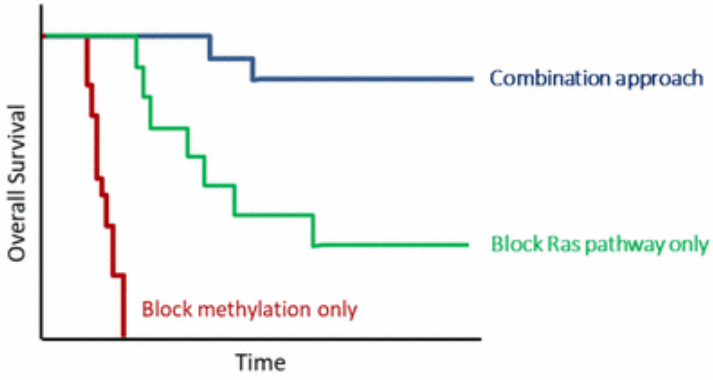
ORAL RIGOSERTIB DEVELOPMENT PROGRAM

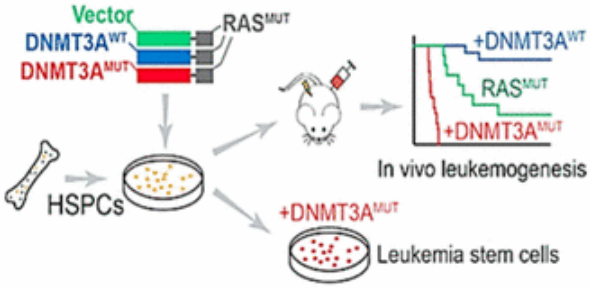
COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

Preclinical evidence supports synergism of rigosertib + azacitidine combination

AML Mouse Model

Validation of combination approach

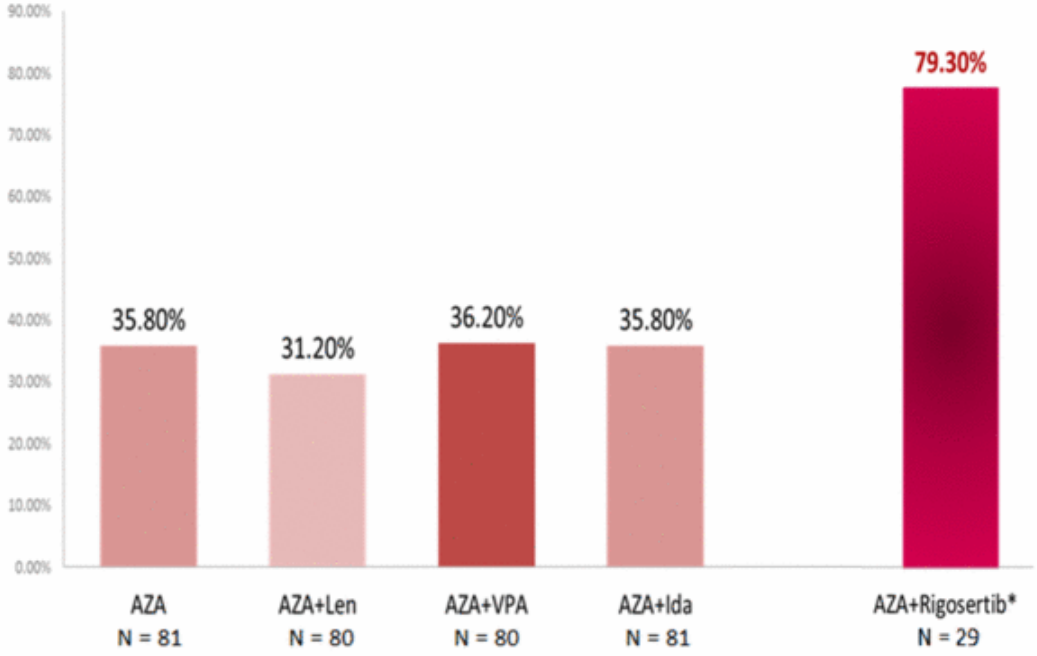




Lu et al., 2016 Cancer Cell

COMBINATION OF ORAL RIGOSERTIB AND STANDARD DOSE AZACITIDINE: VARIOUS 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

HMA NAÏVE ≥ 840MG/DAY (NOT TREATMENT NAÏVE)

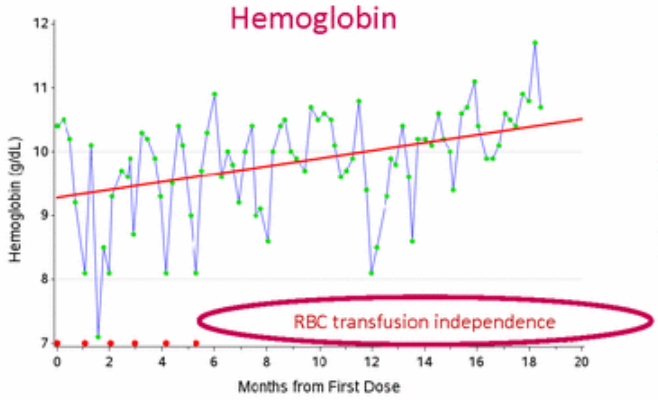
Evaluable for response	29*
Overall response per IWG 2006	26 (90%)
CR+PR	10 (34%)
Complete remission (CR) Partial remission (PR) Marrow CR + Hematologic Improvement Hematologic Improvement alone Marrow CR alone Stable disease Progression	10 (34%) 0 5 (17%) 3 (10%) 8 (28%) 3 (10%) 0
Median duration of 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

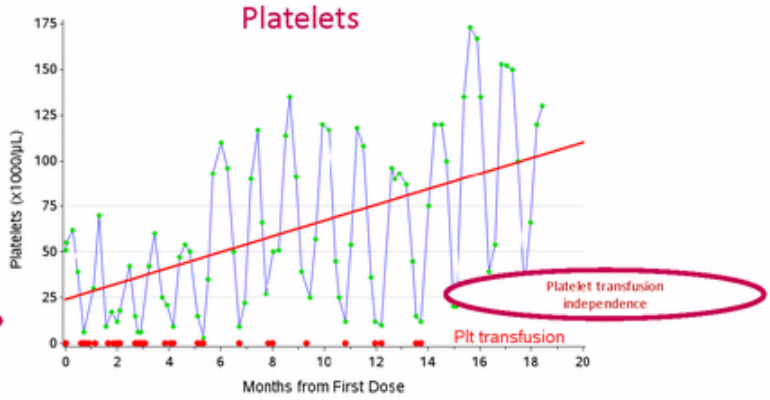
**** Includes 2 patients treated with non-HMA, prior chemotherapy***

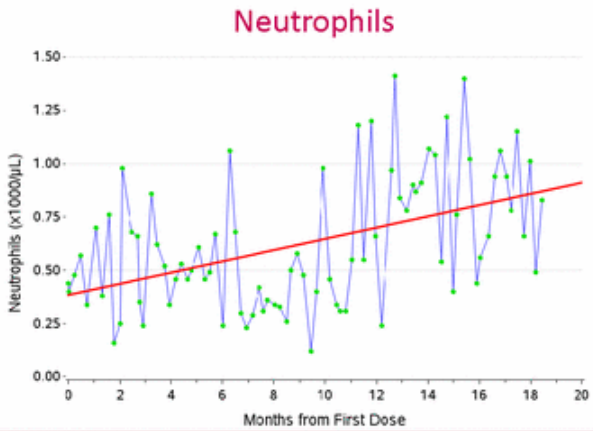
Navada et al: *Blood* 2018 132:230 and EHA June 2019

COMBINATION THERAPY MAY LEAD TO TRANSFUSION INDEPENDENCE

Single patient case data:*





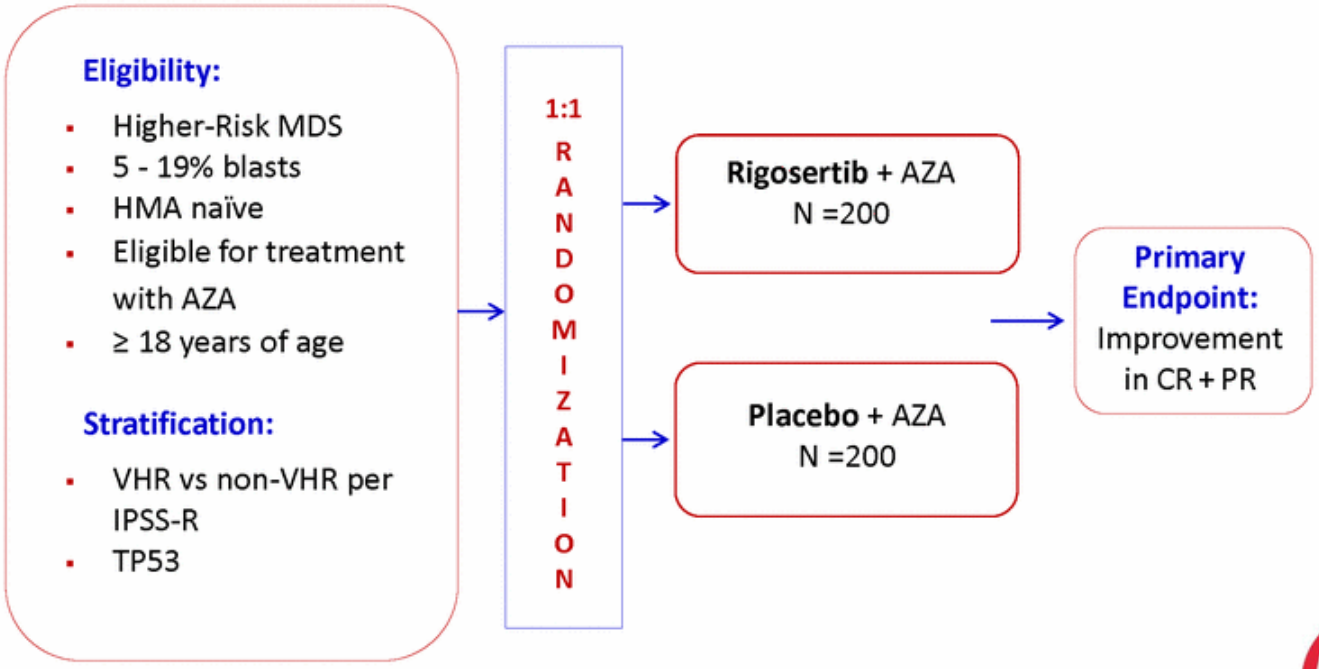


- 12 cycles of AZA – stable disease
- RBC and platelet transfusions
- Blasts 7%
- Monosomy 7
- Runx-1
- AZA + RIG in 09-08 for 20+ months
- Complete remission
  - RBC transfusion independence
  - <5% blasts
  - PB CR criteria

** Individual patient response data may vary*

PHASE 3 PROPOSED DESIGN FOR TREATMENT NAÏVE HR MDS

Phase 3, multi-center, international, randomized, double-blind, placebo- controlled study of oral rigosertib + injectable azacitidine (AZA) versus injectable AZA plus oral placebo in patients who are hypomethylating agent treatment-naïve with higher-risk myelodysplastic syndrome (MDS)

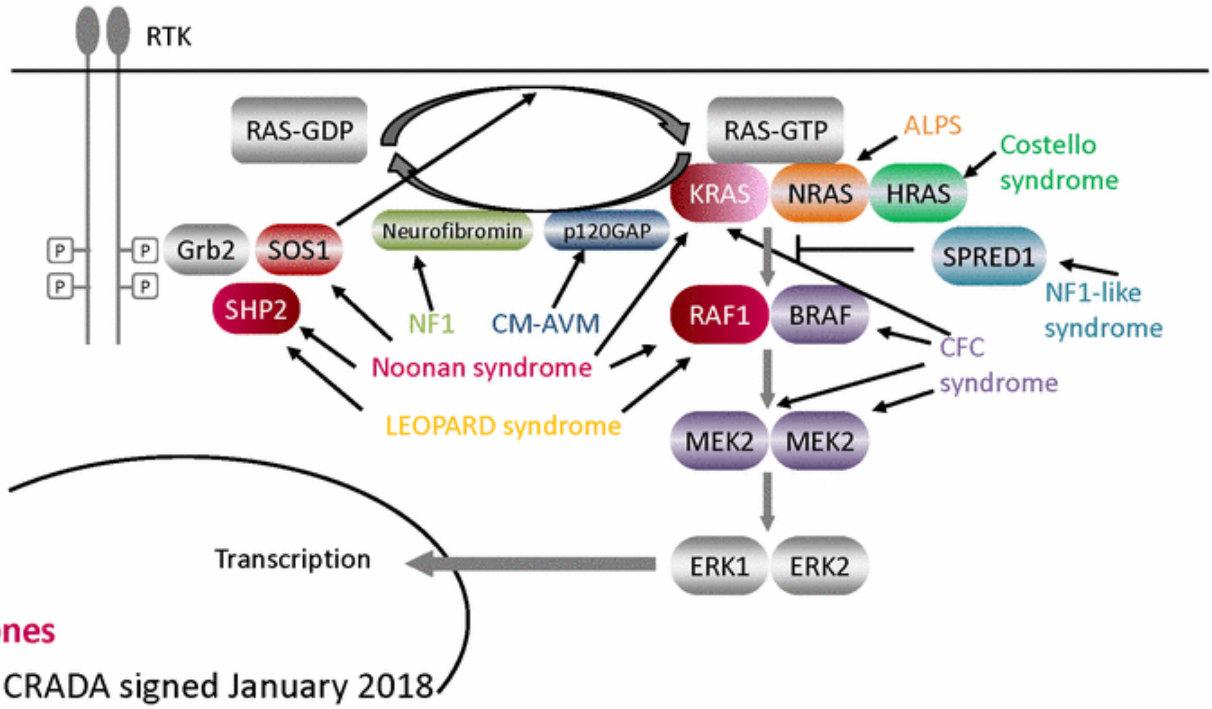


COMBINATION THERAPY: NEXT STEPS AND TIMELINES

Step	Start	Status	Remarks
Phase 2 expansion *Fully enrolled*	Q1-2017	Q2-2018	▪ Dose and schedule of 1120 mg daily dose presented at ASH 2018*
Phase 3 protocol	Q1-2018	Under FDA Review	▪ Protocol and SPA submitted for FDA agreement in Dec 2018
Phase 3 trial	Following FDA Decision	2022 Completion Anticipated	▪ Rapid enrollment expected ▪ Response endpoint can be achieved in <6-9 months after patient is enrolled

*Dose justification based on oral rigosertib optimal transfusion independence rate data in Lower-Risk MDS (ASH 2017)

RASOPATHIES: RIGOSERTIB FOR RARE PEDIATRIC CANCERS



Milestones

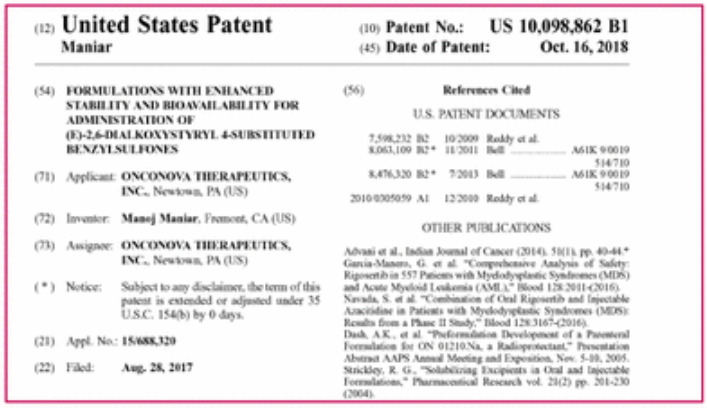
- NCI CRADA signed January 2018
- UCSF non-clinical program initiated
  - Funded by LLS
- JMML clinical program anticipated

Goal is a Pediatric Voucher

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, Europe
- **New issued 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

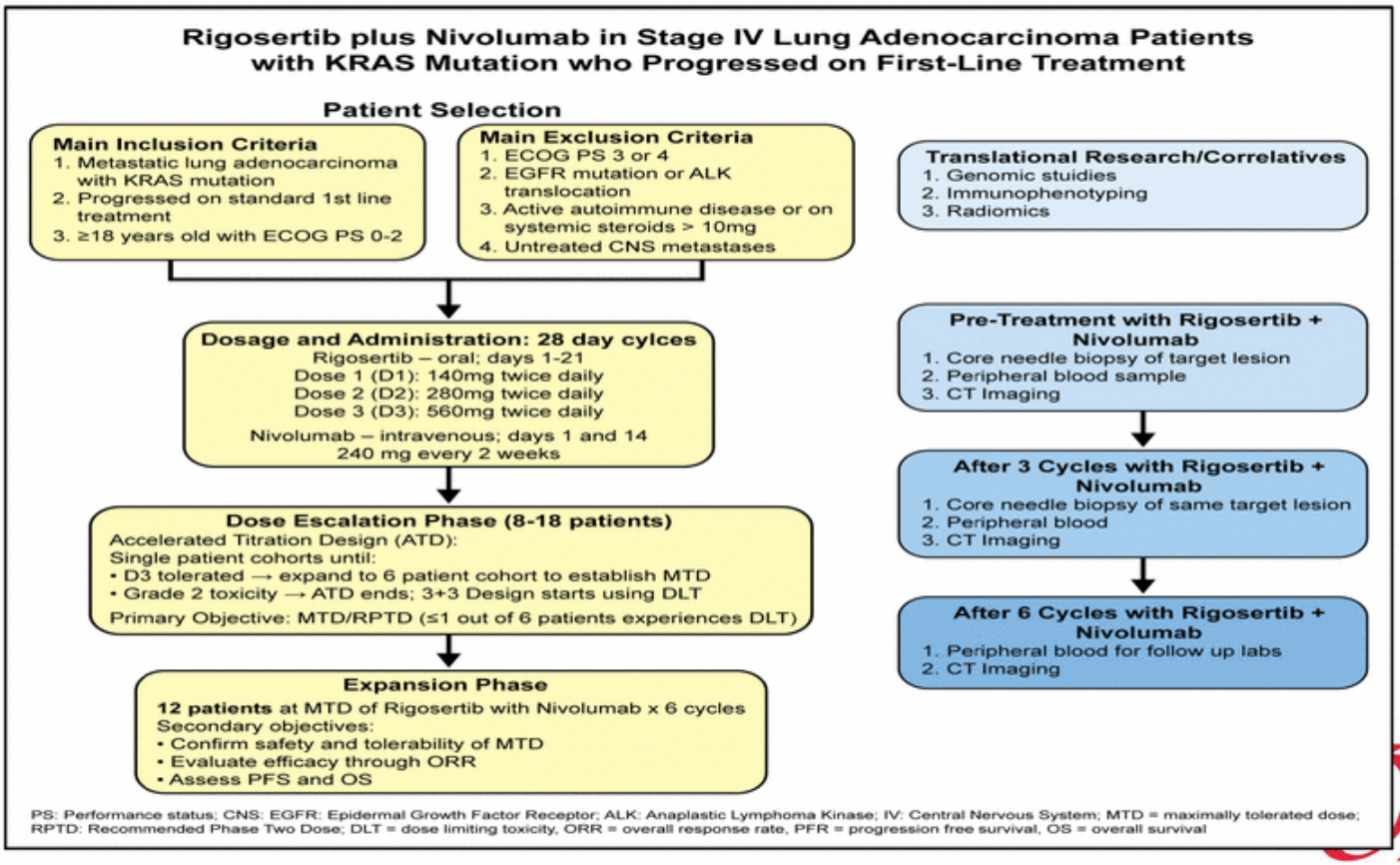
7,598,232	B2	10/2009	Reddy et al.	
8,063,109	B2 *	11/2011	Bell	A61K 9/0019 514/710
8,476,320	B2 *	7/2013	Bell	A61K 9/0019 514/710
2010/0305059	A1	12/2010	Reddy et al.	

OTHER PUBLICATIONS

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).

Phase 1 Study: Rigosertib and PD-1 in Advanced Kras+ NSCLC

PI: Raj Veluswamy, MSSM



PS: Performance status; CNS: EGFR: Epidermal Growth Factor Receptor; ALK: Anaplastic Lymphoma Kinase; IV: Central Nervous System; MTD = maximally tolerated dose; RPTD: Recommended Phase Two Dose; DLT = dose limiting toxicity, ORR = overall response rate, PFR = progression free survival, OS = overall survival

ON 123300: NEXT GENERATION CDK4/6 INHIBITOR

Also targets ARK5 (NUAK1)

Differentiation for a Competitive Field

- Recently launched Ibrance®, Kisquali® and Verzenio® have been hailed as potential 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

Partnership with HanX Biopharmaceuticals

- License for Greater China
  - Onconova retains ROW rights
- HanX to fund IND-enabling studies
- Upfront, milestones, royalties
- HanX a specialty Oncology company
  - Phase 1 stage PD-1 checkpoint antibody
  - Checkpoint blockade and CDK inhibition believed to be synergistic
- Pre-IND consultation with the FDA
  - Guidance for manufacturing
  - Development plan for an IND application
- Next Milestone is IND
- US IND submission anticipated Q4-2019

ONCONOVA BUSINESS DEVELOPMENT OPPORTUNITIES

Patent-protected, differentiated small molecule compounds

Compound	Target	Stage	Next Step	Other Agents	Patents	Licensing Territories Available
Clinical Stage						
Rigosertib	▪ RAS pathway ▪ MDS initial indication	Phase 3	INSPIRE Pivotal Readout of Data 1H 2020	HMAs	Worldwide issued and pending to 2037	Europe, US, Canada, Middle East, Africa, Southeast Asia, Australia, New Zealand
Advanced pre-IND stage						
ON 123300	CDK4/6; ARK5	Pre-IND	IND Submission anticipated Q4 19	Palbociclib	Issued US, EP	Ex-China rights

COMPANY CAPITALIZATION

Outstanding Securities	As of 9/12/19
Common Stock	5,998,524
Options outstanding (WAEP: $66.65)	404,957
Warrants (WAEP: $9.113)	5,504,722*

**5.13 million warrants will expire by 12/31/19 if unexercised*

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*	Univ of Calgary, Scripps Clinic & Research Institute, Novartis, Ortho Biotech Products
	Mark Guerin *Chief Financial Officer*	Barrier Therapeutics, Cardiokine, PricewaterhouseCoopers
	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


ONCONOVA
THERAPEUTICS
info@onconova.us