ONCONOVA THERAPEUTICS

# CORPORATE PRESENTATION

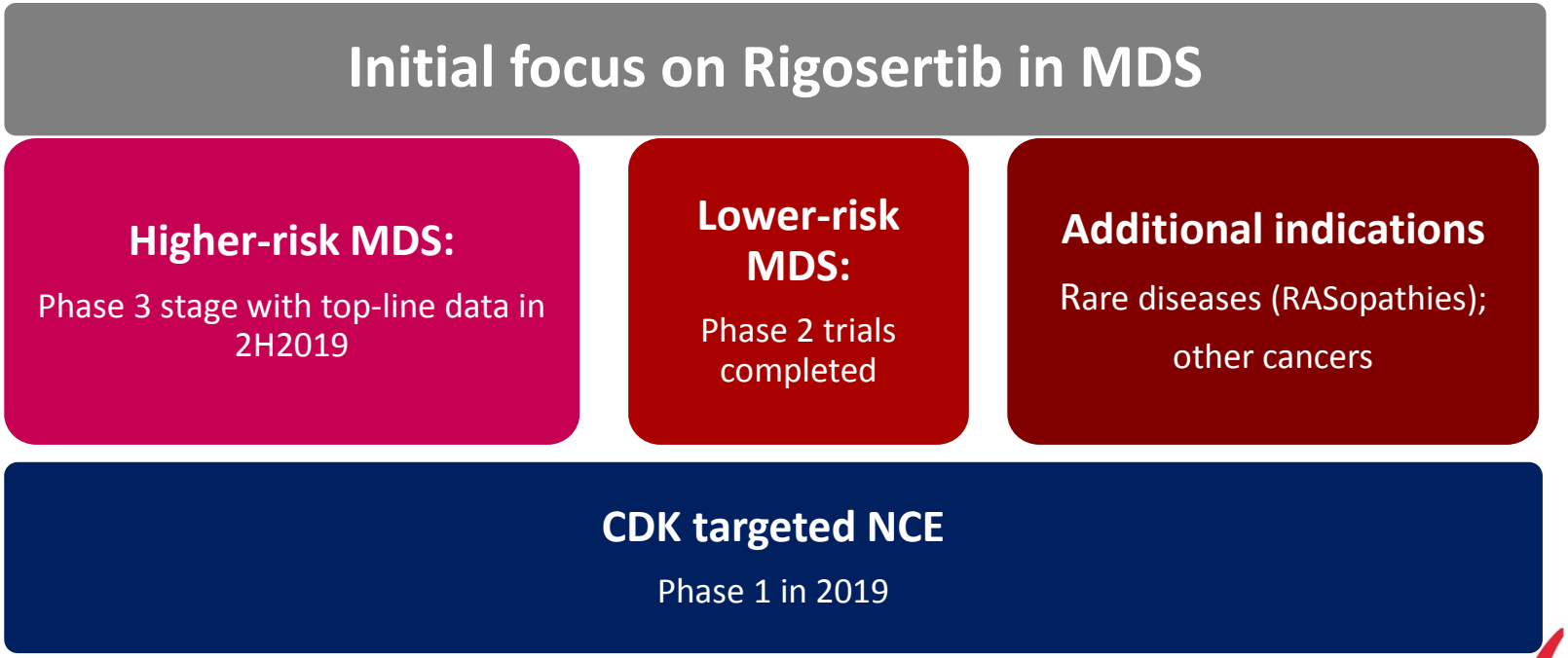
**January 2019 | Nasdaq: ONTX**

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. 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.

# ONCONOVA THERAPEUTICS, INC.

- Founded in 1998; IPO in 2013 (Nasdaq: ONTX)
- Rigosertib partnered in Japan and Korea (SymBio) and Latin America (Pint)
  - Additional partnerships, including China, anticipated



# PORTFOLIO: RIGOSERTIB AND OTHER OPPORTUNITIES

**Lead**

- Phase 3 INSPIRE trial progressing to completion after promising interim analysis and enhanced powering through adaptive design
- Trial completion projected in H2-2019

**Oral**

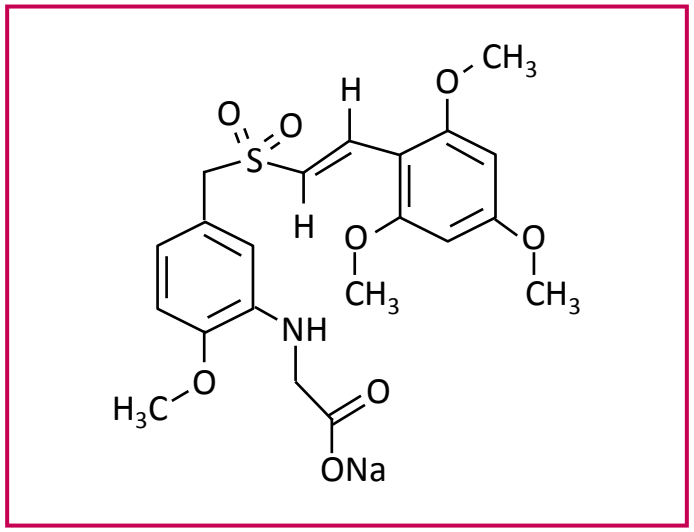
- Oral rigosertib provides two large-market opportunities
- Combination trial for first-line high-risk MDS Phase 3 protocol under FDA Special Protocol Assessment Review

**More**

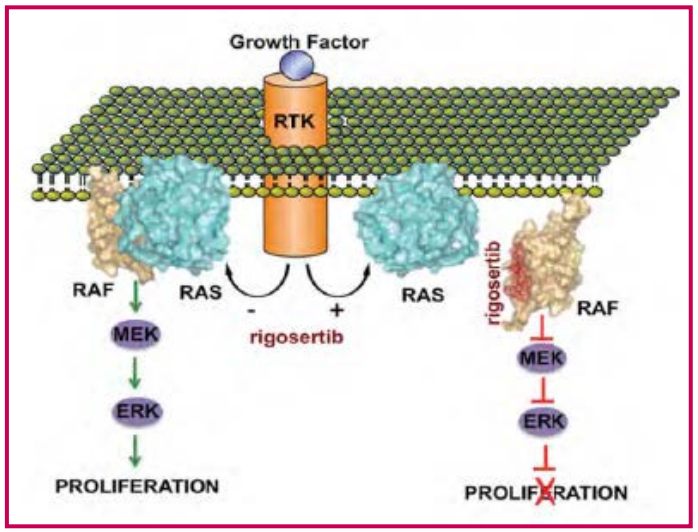
- NCI funded RASopathies trial for rare pediatric indications
- New CDK inhibitor presents opportunities for the future

# ABOUT RIGOSERTIB: PHASE 3 STAGE LEAD DRUG

**Patent protected new chemical entity (NCE)**




**RAS targeted novel mode of action**



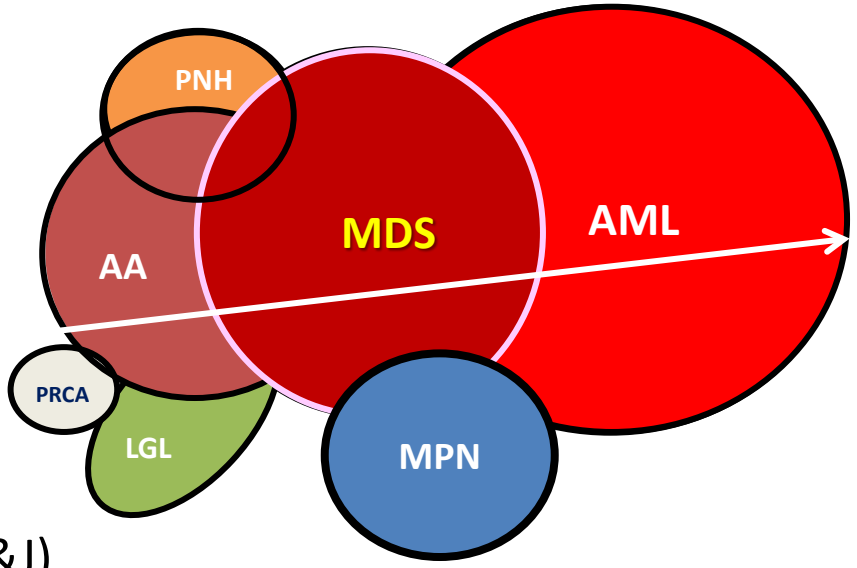

**Two formulations in clinical trials worldwide**

IV product for infusion

Oral soft gel capsules

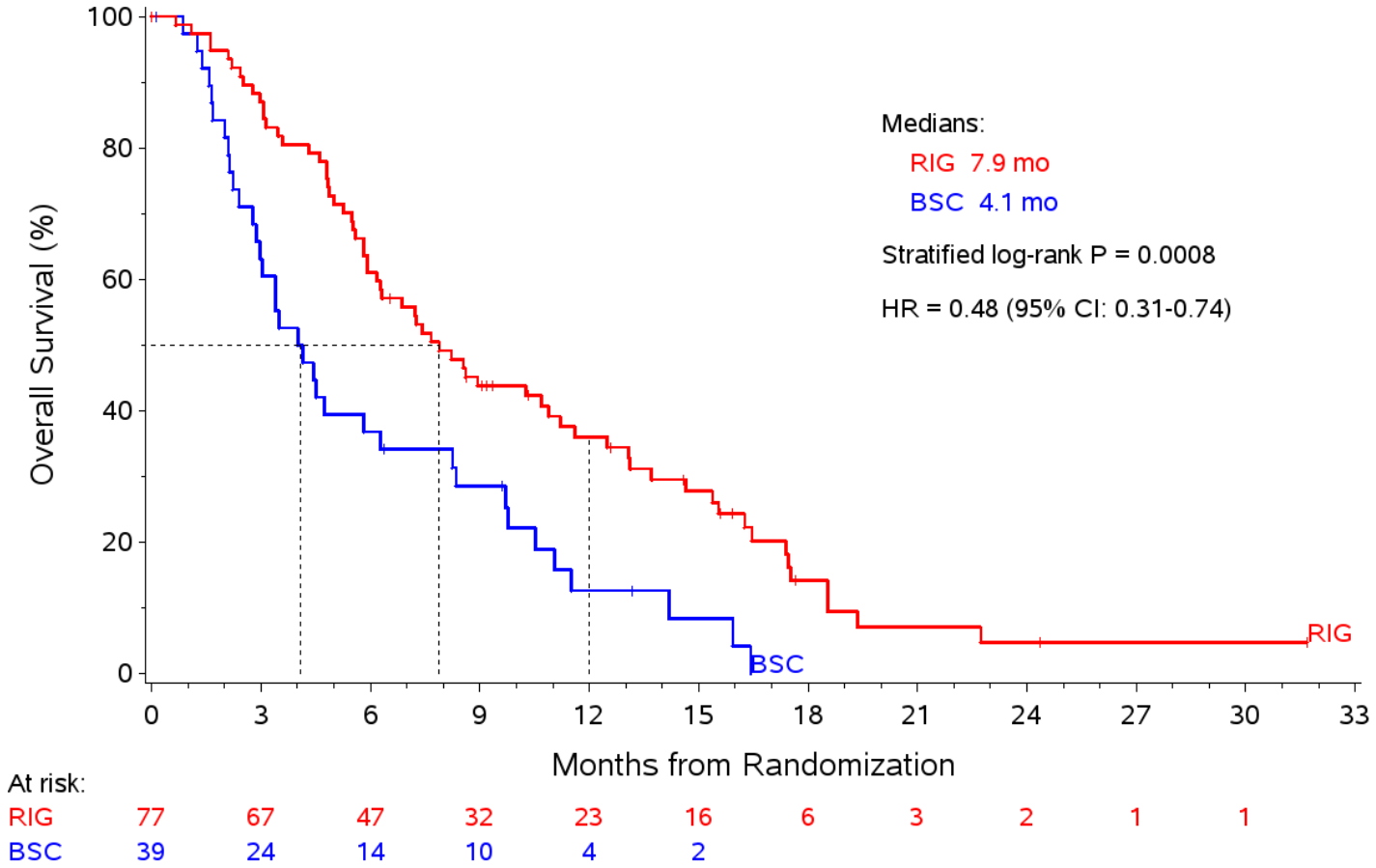
# MDS IS RELATED TO OTHER BONE MARROW DISEASES

- 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
  - Vidaza (Celgene); Dacogen (Eisai/J&J)
  - Approved >decade ago; now off-patent
  - No approved therapy following HMA failure
  - New therapy could have $billions opportunity



# STUDY 04-21 : PROPOSED PATIENT POPULATION FOR INSPIRE

(≤9 HMA DoT; <82 years)



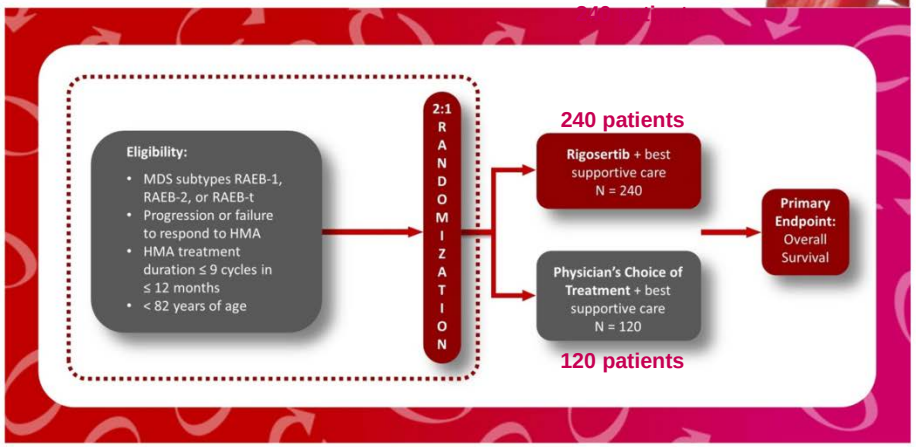
# INSPIRE PHASE 3 TRIAL RESULTS EXPECTED IN 2019

## The Pivotal MDS **INSPIRE** Trial is Now Recruiting Patients

**IN**ternational **S**tudy of **P**hase III **I**ntravenous **R**igos**E**rtib

### STUDY DESCRIPTION

A Phase 3, international, randomized, controlled study of Rigosertib + best supportive care versus physician's choice of treatment + best supportive care in patients with myelodysplastic syndrome (MDS) after failure of a hypomethylating agent (HMA).




### PRIMARY ENDPOINTS

Overall survival in the intention-to-treat population and in patients with very high risk per the Revised International Prognostic Scoring System (Greenberg et al, *Blood* 2012).

### INTERNATIONAL TRIAL

More than 170 trial sites

**INSPIRE start**
December 2015

**Interim Analysis**
January 2018

***Trial size increased after "promising" survival signal***

**Top-line Data**
*H2-2019 (projected)*

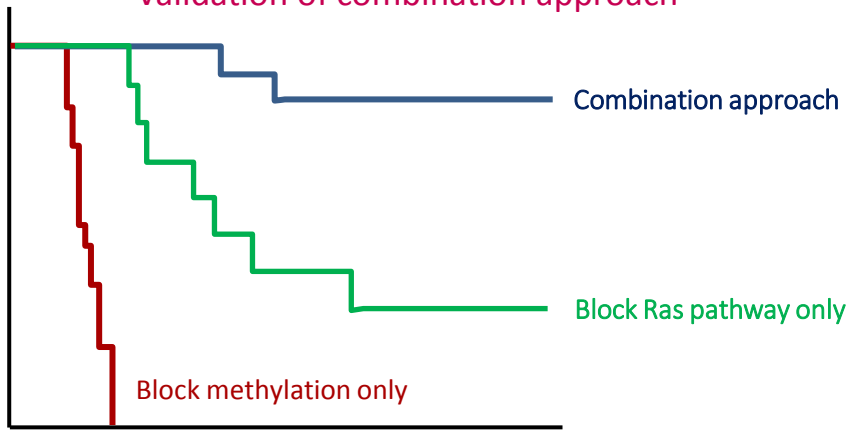
- **Interim analysis was conducted after 88 events: January 2018**
- **Topline data after 288 events expected in H2-2019**
- **Trial running at >170 sites in 22 countries on 4 continents**

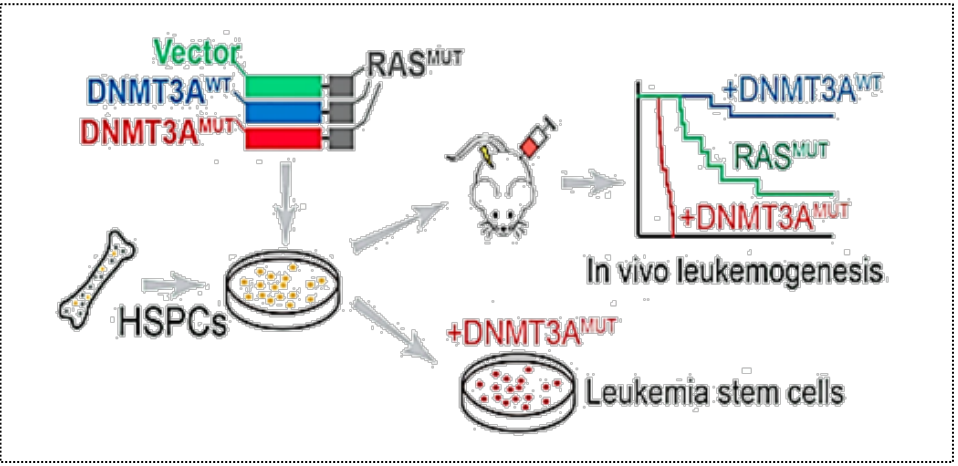
# COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

**Preclinical evidence supports synergism of rigosertib + azacitidine combination**

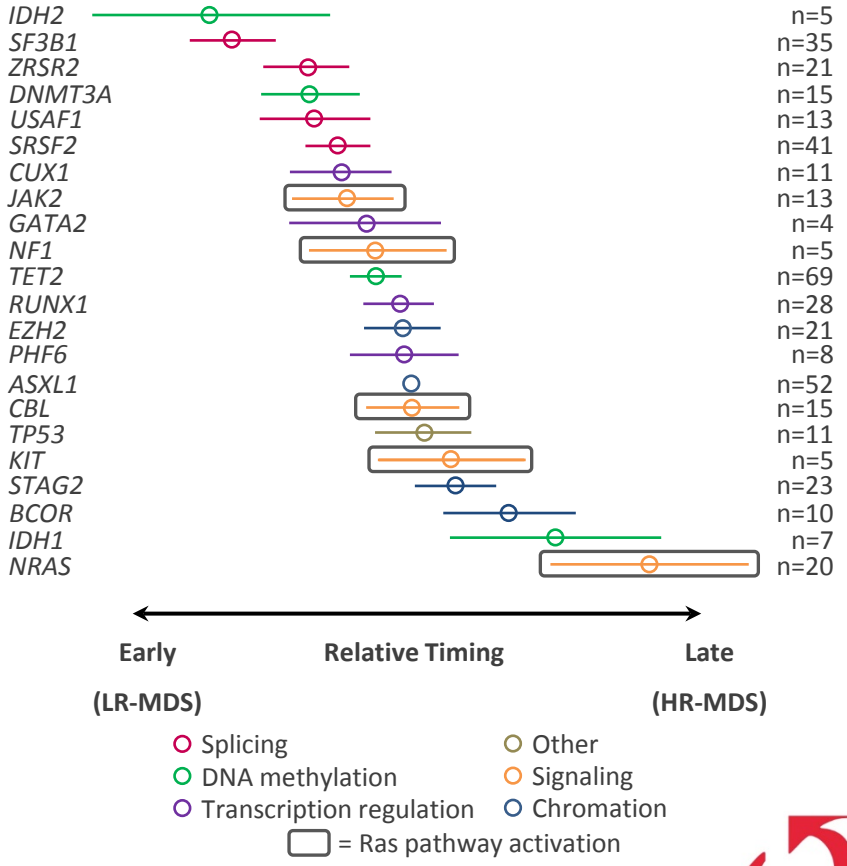
## AML Mouse Model

Validation of combination approach[1]




## Temporal Order of Gene Mutations in 107 MDS Patients[2]




*1. Lu et al., 2016 Cancer Cell*

*2. Adapted from Papaemmanuil et al., 2013 Blood*

# HMA NAIVE ≥ 840MG/DAY

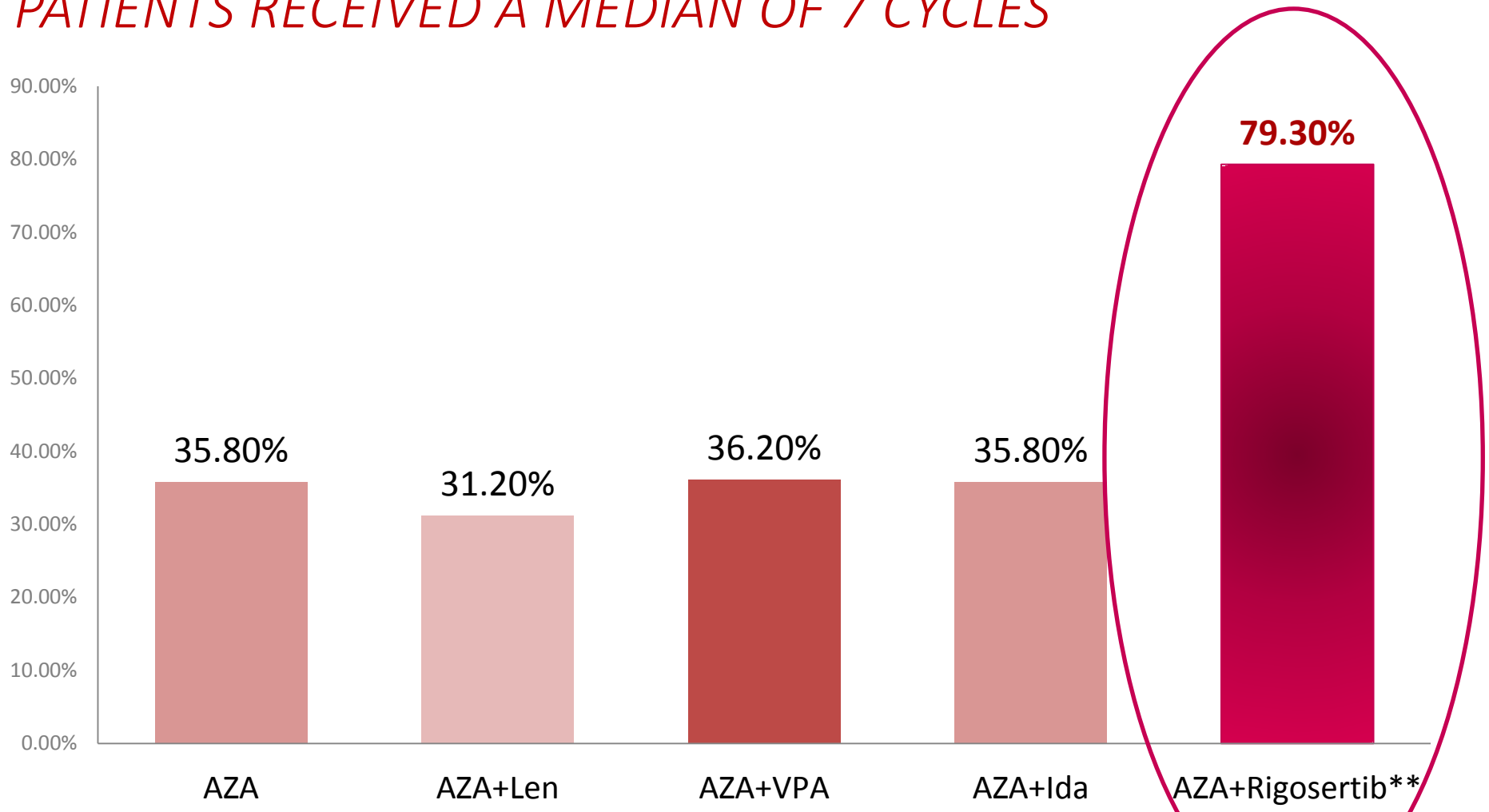
*EFFICACY*

| | |
|---|---|
| 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 treated with non-HMA, prior chemotherapy***

# RESPONSE RATE (CR/PR/mCR*)

## *PATIENTS RECEIVED A MEDIAN OF 7 CYCLES*




***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***

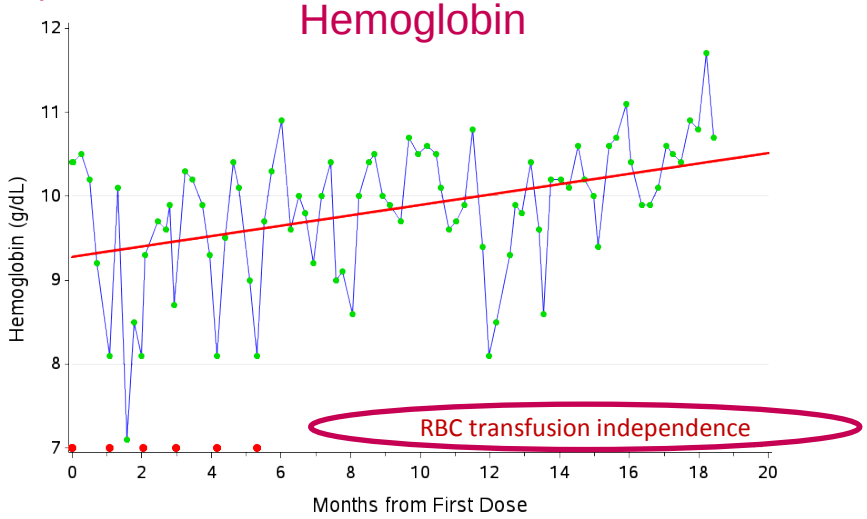
*Lionel Adès et al: ASH; 2018

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

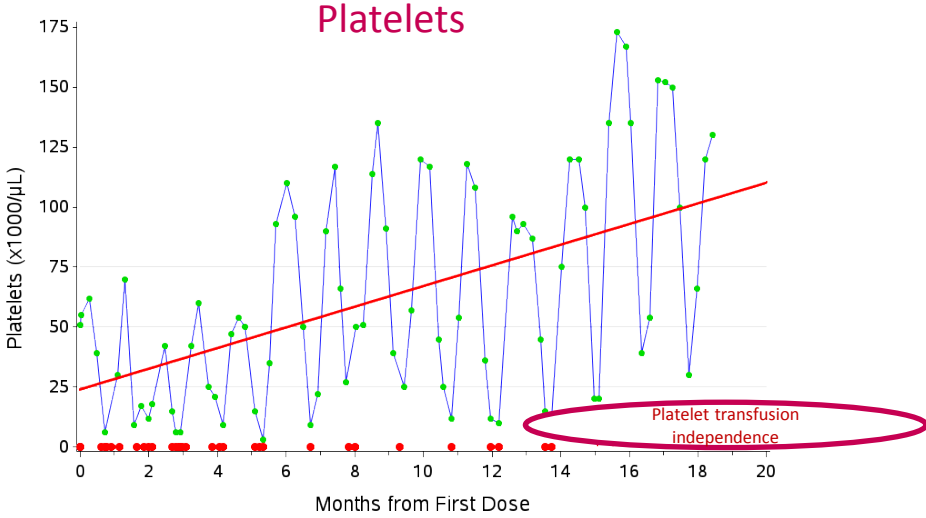
# COMBINATION THERAPY MAY LEAD TO TRANSFUSION INDEPENDENCE

*Single patient case data*:*

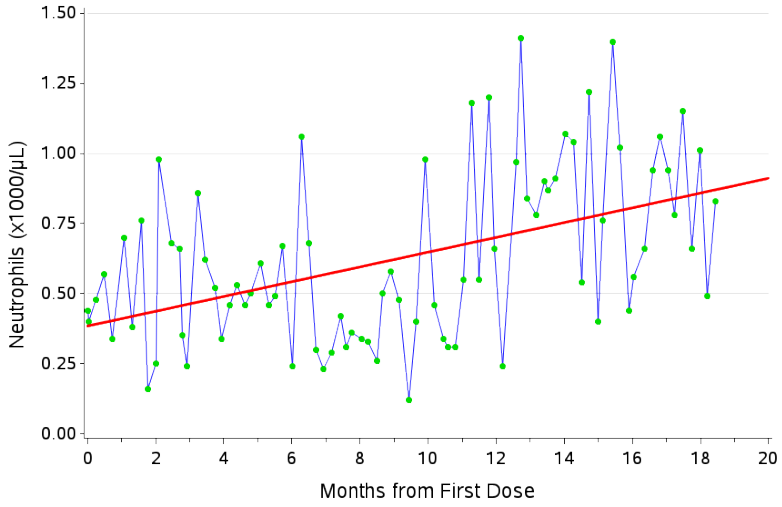
## Hemoglobin




## Platelets




## Neutrophils




- 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*

# SAFETY OPTIMIZATION STRATEGIES

*COMPARISON OF RIGOSERTIB DOSING GROUPS*

| Safety Optimization Strategies | | | |
|---|---|---|---|
| **2nd RIGO dose must be administered at 3 PM (±1 hour) at least 2 hours after lunch to avoid a nocturnal bladder dwell time** | **Oral hydration of at least two liters of fluid per day is encouraged** | **Mandatory bladder emptying prior to bedtime** | **Urine pH approximately 2 hrs after AM dose. Sodium bicarbonate suggested administration of 650 TID if pH tests < 7.5** |

| | | **Safety Optimization Strategies Applied** |
|---|---|---|
| | **Rigosertib 840mg** | **Rigosertib 1120mg** |
| | 42 | 43 |
| **Patients with hematuria** | 19 (45%) | 17 (40%) |
| **Patients with grade 1 or 2 hematuria only** | 14 (33%) | 15 (35%) |
| **Patients with grade 3 hematuria** | 5 (12%) | 2 (5%) |
| **Patients with dysuria** | 18 (43%) | 13 (30%) |
| **Patients with grade 1 or 2 dysuria only** | 13 (31%) | 10 (23%) |
| **Patients with grade 3 dysuria** | 5 (12%) | 3 (7%) |

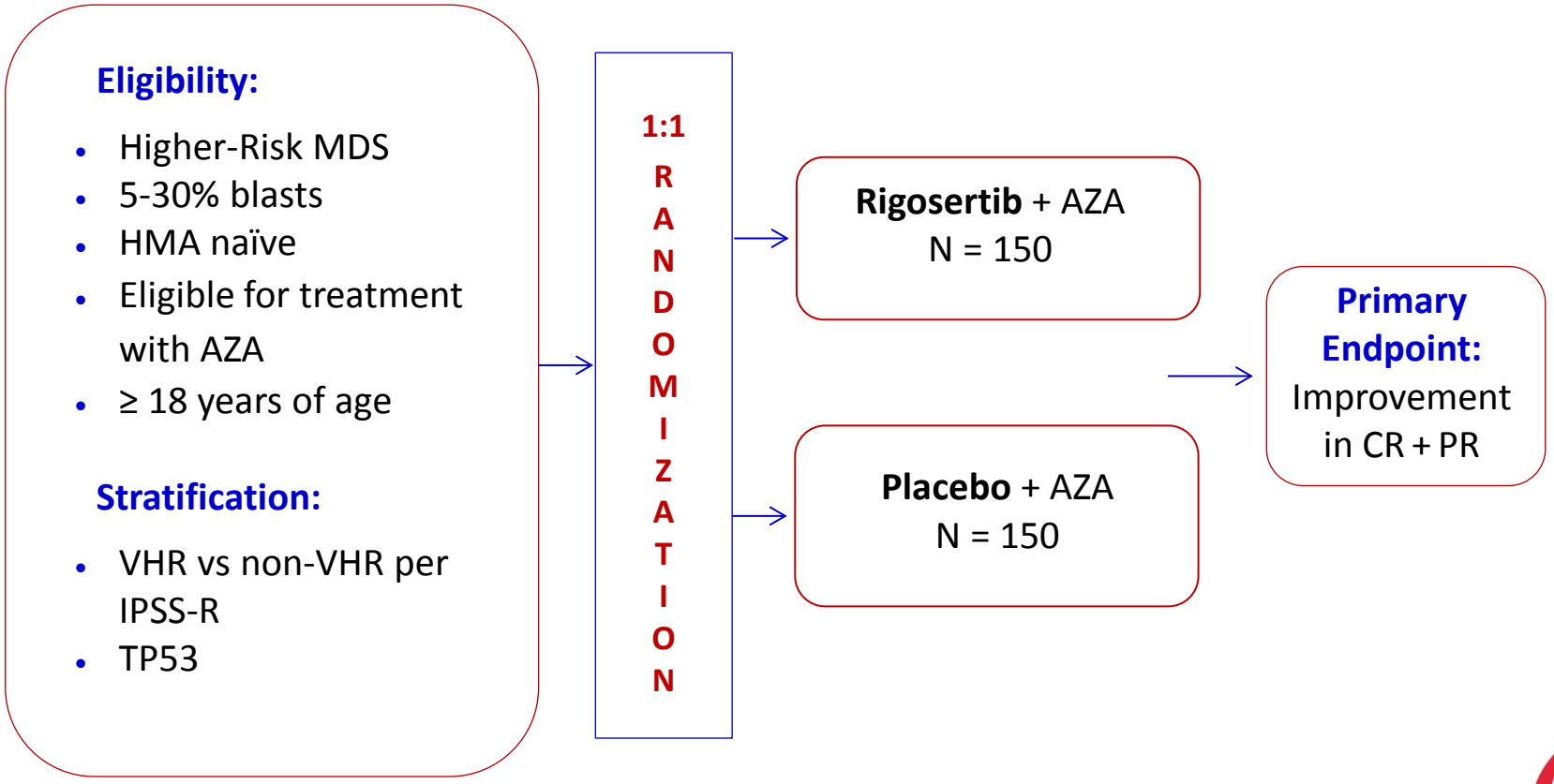
No GR 4 reported

# NEXT PHASE 3 PROGRAM: ORAL RIGOSERTIB IN COMBINATION WITH AZACITIDINE (VIDAZA®) FOR FIRST-LINE MDS

- Overall Response Rate of 90% and a Complete Response rate of 34%in HMA-naive MDS patients oral rigosertib at doses ≥ 840 mg/day administered with AZA in Phase 2 Expansion Study
  - Efficacy of combination demonstrated in both HMA-naive and HMA-refractory MDS patients
  - Safety and tolerability acceptable in the study population
- A pivotal Phase 3 trial in a Treatment-Naïve High-Risk First-line population is being reviewed by the FDA under a Special Protocol Assessment Request

# PHASE 3 DESIGN FOR TREATMENT NAIVE HR MDS (STUDY 09-15)

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)

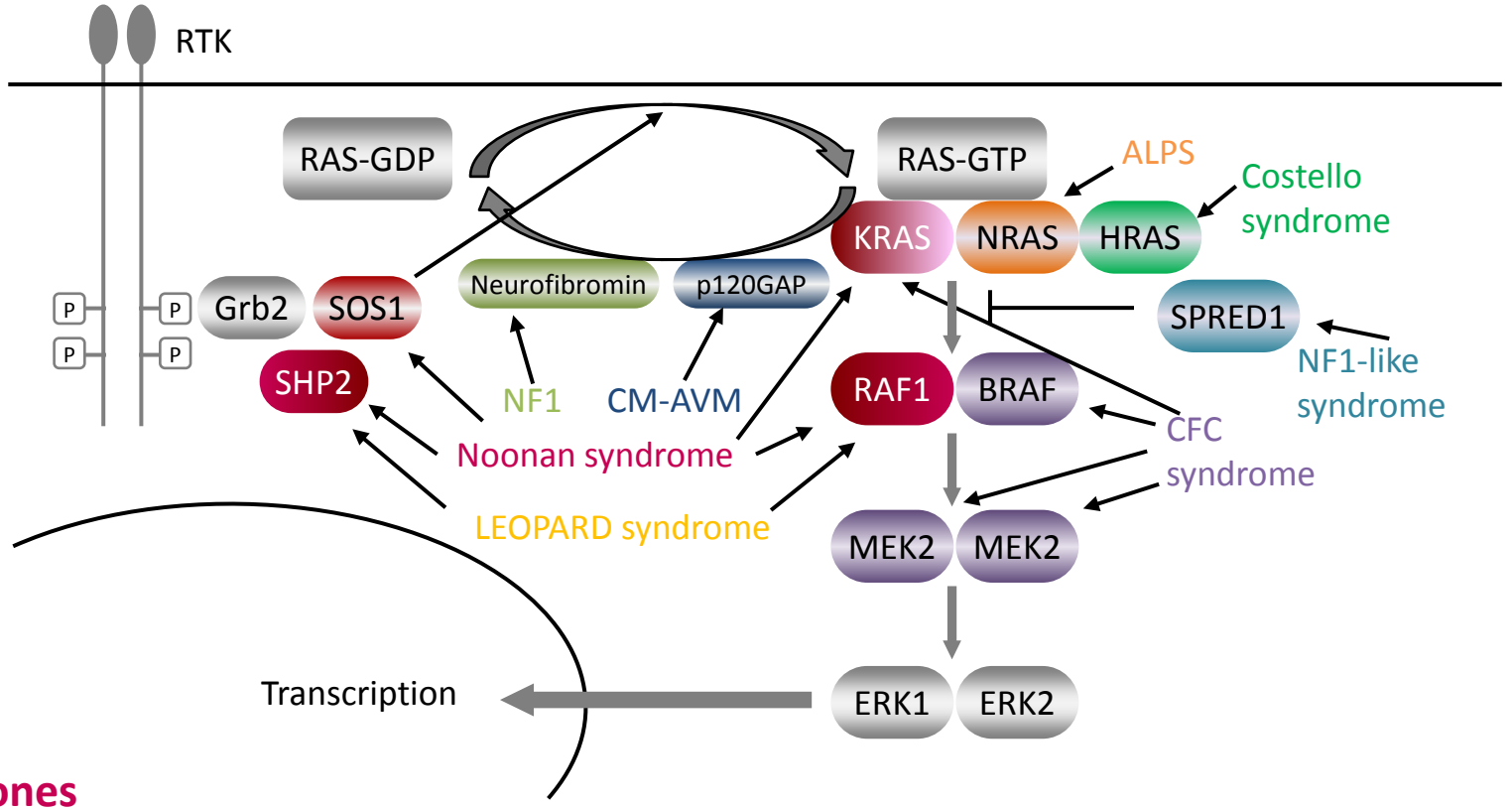


# COMBINATION THERAPY: NEXT STEPS AND TIMELINES

| Step | Start | Complete | Remarks |
|---|---|---|---|
| Phase 2 expansion<br>*Fully enrolled* | Q1-2017 | Q2-2018 | ▪ Incidence of hematuria reduced in the trial<br>▪ Dose and schedule of 1120 mg daily dose explored* |
| Phase 3 protocol | Q1-2018 | Q4-2018 | ▪ Protocol and SPA submitted for FDA approval in Dec-18 |
| SPA Review by FDA<br>Decision by FDA | Q1-2019 | Q1-2019 | ▪ 01-Feb-19 – Start of 45 calendar day review period by FDA<br>▪ Mid Mar-19 – Approval or Non-approval Letter of SPA by FDA *(Note: 45 day review period may take longer if FDA decides to include external advisors into review process)* |
| Phase 3 trial | 2019 | 2022 | ▪ Rapid enrollment expected<br>▪ All patients to receive active therapy<br>▪ 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 DISEASES



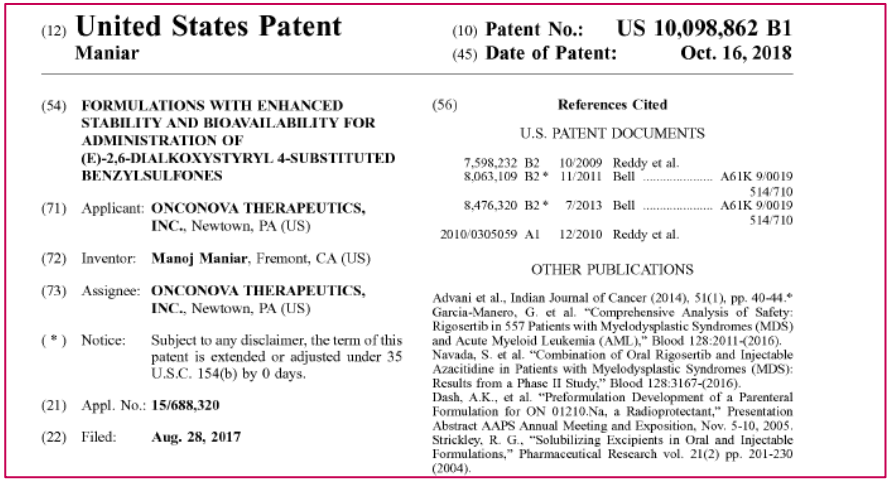

## Milestones

- NCI CRADA signed January 2018
- Potential for first patient in H1-2019
- UCSF non-clinical program initiated
  - Funded by LLS
- JMML clinical program could initiate in 2019

# 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 and Japan
- **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).

# ON 123300: NEXT GENERATION CDK4/6 INHIBITOR

Also targets ARK5 (NUAK1)

## Differentiation for a Competitive Field

- Recently launched Ibrance®, Kisqualí® 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 anticipated in H1-2019

***IND enabling toxicology and CMC studies underway***

# 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**<br>• **MDS initial indication** | **Phase 3** | **Top-line data in 2019** | **Only HMAs approved for MDS** | **Worldwide issued and pending to 2037** | **Asia, except Japan and Korea**<br>**Europe**<br>**North America** |
| ***Advanced pre-IND stage*** | | | | | | |
| **ON 123300** | **CDK4/6; ARK5** | **IND in 2019** | **Toxicology underway** | **Palbociclib** | **Issued US, EP** | **Ex-China rights** |
| ***Pre-clinical stage*** | | | | | | |
| ON 150030 | FLT3 + Src | Pre-clinical | Animal studies | Quizartinib | Issued US, EP | Worldwide |
| ON 1231320 | PLK2 | Formulation | Pre-IND | Volasertib | Issued | Worldwide |
| ON 108600 | CK2 | Formulation | Pre-IND | CX-4945 | Issued | Worldwide |
| ON 146040 | PI3K $\alpha/\delta$ | Pre-clinical | Toxicology | IPI-145 | In process | Worldwide |

# FINANCIAL DETAILS & SUMMARY

| Onconova founded in 1998; public since 2013 | | | |
|---|---|---|---|
| **Ticker** | Nasdaq ONTX | **Debt** | $0 |
| **Stock Information** | ▪ 5.7 million common shares outstanding<br>▪ Public float ~95%<br>▪ 2018 average daily volume 100,000 shares | **Cash** | Cash and cash equivalents of $22.4 million as of 09-30-2018 |
| **Ownership** | 683 Capital, EcoR1 Capital, Armistice Capital, Tyndall, Sabby; insiders including Board and management | **Burn-rate** | $5.8 million per quarter over the past 4 quarters |
| **Analyst Coverage*** | H.C. Wainwright, Laidlaw, Maxim, Dawson James, Van Leeuwenhoeck Research (VLR) | **Partnerships** | ▪ Rigosertib is partnered with SymBio Pharmaceuticals in Japan/Korea and Pint Pharma in Latin America<br>▪ CDK 4/6 & ARK-5 compound ON 123300 partnered with HanX for Greater China<br>▪ Onconova retains rights to the rest of the world |

**Reports available upon request*

# MANAGEMENT TEAM

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

# RECENT/UPCOMING CATALYSTS AND PRESENTATIONS

## 4Q2018

- Expansion and Extension of Rigosertib Patent Portfolio
- ASH 2018 Oral Presentation of Expansion Phase 2 Combination Trial Data
  - Phase 3 trial protocol and special protocol assessment (SPA) request submitted

## 2019

- RASopathies Pediatric Oncology program
  - Initiation of clinical trial at NCI
- CDK 4/6+ARK5 Inhibitor program
  - IND process and start of Phase 1 program
- INSPIRE Phase 3 Trial
  - Full enrollment and top-line data

## 2018-2019

- Anticipated Business Development Activities
  - Additional regional alliances for Rigosertib
  - Additional alliances for CDK and other pre-clinical programs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