Issuer Free Writing Prospectus
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June 20, 2016

ONCONOVA THERAPEUTICS

ONTX Corporate Presentation

June 2016

Free Writing Prospectus Statement

- This presentation highlights basic information about us and the offering. Being a summary document, this slide deck does not contain all the information that you should consider before investing.
- We have filed a registration statement (including a preliminary prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the preliminary prospectus in the registration statement (including the risk factors described therein) and other documents, including the Company's Form 10-Ks and Form 10-Q, that we have filed with the SEC for more complete information about us and the offering.
- You may get these documents for free by visiting the "Search EDGAR" section on the SEC web site at http:/ /www.sec.gov. The preliminary prospectus, dated June 20, 2016, is available on the SEC website. Alternatively, we or the dealer-manager for this offering, Maxim Group LLC will arrange to send you a preliminary prospectus if you contact Maxim Group LLC, Prospectus Department, 405 Lexington Ave., New York, NY, 10174; Telephone: (212)-895-3745; Email: syndicate@maximgrp.com.

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 in 1998; proprietary novel therapeutics
- Headquarters: Newtown, PA
- NASDAQ Ticker Symbol: ONTX; IPO July 2013
  - Citi, Leerink, Piper, Janney, ~$80 Million raised
- MCAP: ~$15M
- Cash sufficient to get into Q1-2017

Investment Highlights

- **Established company with differentiated late-stage product**
  - Value proposition with near-term catalysts and inflection points
- **Large commercial opportunity in pre-leukemic disease called MDS***
  - MDS is unmet medical need with high incidence (>59K patients/year)
  - Celgene and Eisai built major MDS product franchises yielding >$500M combined North American sales in 2012
  - Currently no approved drugs for MDS patients after HMA** failure
- **Patented chemistry platform focusing on novel cancer drugs**
  - Rigosertib, lead drug, is now in a pivotal global Phase 3 INSPIRE trial
    - IP protection (composition coverage) and Orphan Drug Designation in MDS
    - Rigosertib partnered in Japan/Korea; Onconova retains U.S. and other rights
    - Partnering efforts underway in sync with Phase 3 trial
  - Deep pipeline beyond lead product

Myelodysplastic Syndromes, a hematology/oncology orphan indication affecting elderly patients
***HMA: Hypomethylating Agents; two approved agents: Azacitidine (Vidaza®) and Decitabine (Dacogen®); both are now generic*

Management Team

Ramesh Kumar, Ph.D.
President & CEO
Co-founder

- DNX
- Bristol-Myers Squibb
- Baxter
- Kimeragen
- Princeton University

Steven M. Fruchtman, M.D.
Chief Medical Officer

- Novartis
- Janssen
- Syndax
- Allos Therapeutics
- Spectrum Pharmaceuticals
- Mount Sinai

Mark Guerin, CPA	Chief Accounting Officer	Barrier Therapeutics, Cardiokine, Pine Hill
Manoj Maniar, Ph.D.	Senior VP, Product Development	Alcon, SRI
Wolfgang Meyer, Ph.D.	VP Regulatory Affairs GM, Onconova GmBh	Amgen, Micromet, GPC, Fujisawa
Michael Petrone, M.D.	VP Clin. Dev. Medical Affairs and Pharmacovigilance	GSK, Roberts, GPC

Board of Directors

Michael B. Hoffman Chairman	**Partner, Riverstone Holdings LLC**
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Jerome E. Groopman M.D.	**Chief of Experimental Medicine at the Beth Israel Deaconess Medical Center**
Ramesh Kumar Ph.D. President and CEO	**President and CEO, Onconova Therapeutics Inc.**
Viren Mehta Pharm.D.	**Managing Member of Mehta Partners**
E. Premkumar Reddy Ph.D. Founder, Lead Scientific Advisor	**Professor in the Department of Oncological Sciences & Department of Structural & Chemical Biology at the Mount Sinai School of Medicine**
Jack E. Stover	**Interim President & CEO, Interpace Diagnostics Group, Inc.**
James J. Marino, Esq.	**Former partner at Dechert LLP**

Onconova Product Pipeline

Program	MOA*	Indication	Preclinical	Phase 1	Phase 2	Phase 3	NDA/MAA
Single-agent IV rigosertib	Ras signaling	2nd-line Higher-risk (HR-MDS)	INSPIRE Pivotal Trial; top-line data expected in 2018				Key Focus
Oral rigosertib + azacitidine		1st-line Higher-risk (HR-MDS)	09-08 Phase 2 Trial fully enrolled				
IV Briciclib	eIF4E targeting	Solid tumors	Dose-escalation Phase 1 Trial**				
Recilisib	Targets radiation-induced apoptosis	ARS***	Non-Human Primate Efficacy				*Supported by U.S. Government funds*
ON 123300	ARK5+CDK4/6 Targeting	CDK4/6 overactive tumors	Pre-IND Stage				

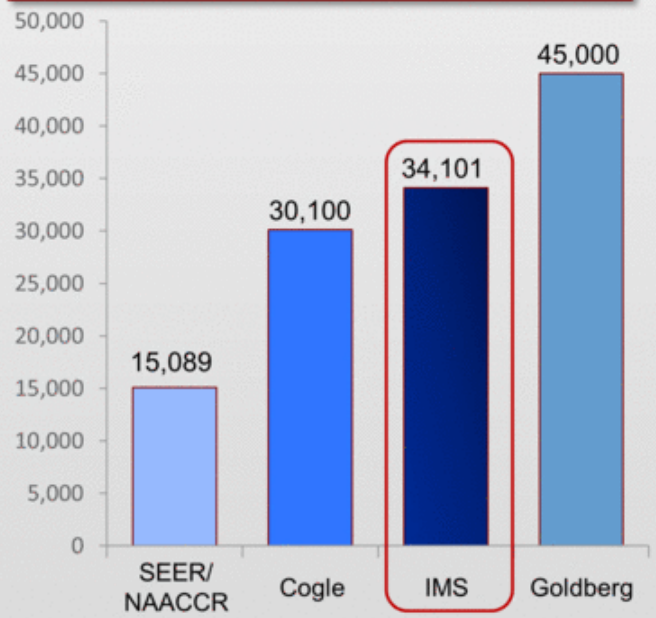
**Mechanism of Action; **Trial on hold pending manufacturing of new product lot; ***Acute Radiation Syndrome*

MDS Epidemiology

Disease affects bone marrow function and can transform into leukemia

Distinct opportunities in lower-risk and higher-risk patients.

Estimated Annual MDS Incidence



- MDS is predominantly disease of the elderly
  - Classified as high- or low-risk disease based on likelihood of progressing to acute myeloid leukemia (AML)
- IMS Identified 34,101 newly diagnosed patients in the U.S. (MAT June 2012)
  - ~47% of the MDS diagnosed patients, mostly low-risk category, are classified as Watch and Wait or not treated
- Incidence of MDS identified and treated patients are growing ~6%
  - Treatment penetration (HMAs, Revlimid) is ~14%; great unmet need

1. 238.7, 238.72 - .76

Sources: Goldberg SL, Chen E, Corral M, Buo A, Mody-Patel N, Pecora AL, Incidence and Clinical Complications of Myelodysplastic Syndromes Among US Medicare Beneficiaries; *J Clin Oncol* 2010 (28):2847-52, IMS Patient Diagnoses Study 2012

Phase 3 Product Rigosertib

- Rigosertib is patent protected through 2026 (IV) and 2028 (combination)
  - Orphan drug designation granted in U.S., EU and Japan
- Phase 3 INSPIRE trial enrolling Higher-Risk MDS* patients
  - Top-line data expected in 2018
- Phase 2 oral rigosertib + azacitidine trial completed enrollment
  - End of Phase 2 meeting with FDA targeted for H2-16
- Rigosertib has extensive clinical trial database
  - Safety data from more than 1,000 patients (IV and oral drug)
  - Randomized Phase 3 trial (ONTIME) in 300 patients
    - Study missed P value for endpoint: published in Lancet Oncology
    - Analysis of ONTIME trial data suggested efficacy in subpopulations of HMA failure patients
    - New global Phase 3 trial based on subpopulations is now underway

*Myelodysplastic syndromes (MDS)

Novel Mechanism of Action

Article

Cell

A Small Molecule RAS-Mimetic Disrupts RAS Association with Effector Proteins to Block Signaling

Sai Krishna Athuluri-Divakar,[1,2] Rodrigo Vasquez-Del Carpio,[1,2] Kaushik Dutta,[3] Stacey J. Baker,[1,2] Stephen C. Cosenza,[1,2] Indranil Basu,[5] Yogesh K. Gupta,[1,2] M.V. Ramana Reddy,[1,2] Lynn Ueno,[4] Jonathan R. Hart,[4] Peter K. Vogt,[4] David Mulholland,[1,2] Chandan Guha,[5] Aneel K. Aggarwal,[1,2] and E. Premkumar Reddy[1,2,*]

[1]Department of Oncological Sciences

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[5]Department of Radiation Oncology, Albert Einstein College of Medicine of Yeshiva University, 1300 Morris Park Avenue, Bronx, NY 10461, USA

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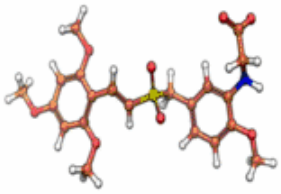
http://dx.doi.org/10.1016/j.cell.2016.03.045



Rigosertib (ON 01910.Na)

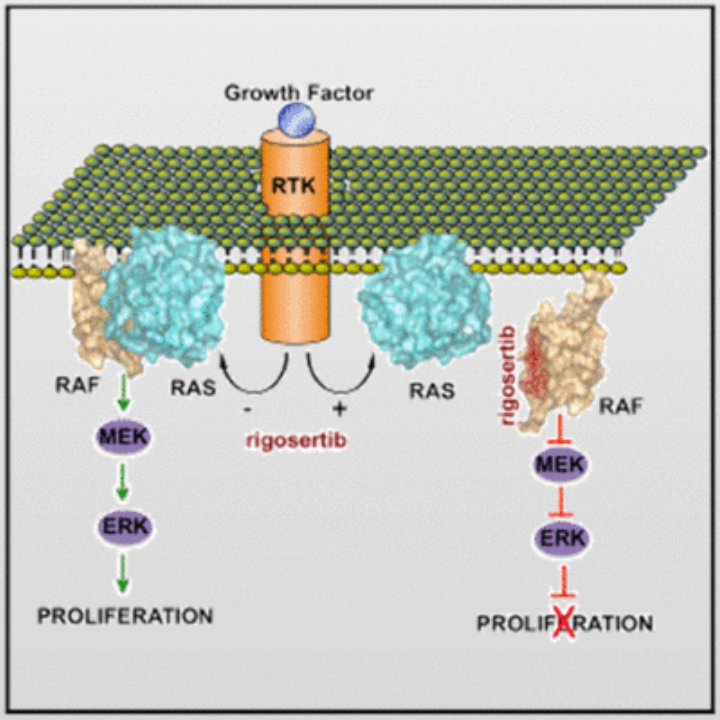
RAS is one of the most frequent (~30%) oncogene activated in a variety of tumors

Rigosertib Mechanism of Action is Directed Against RAS

Rigosertib acts as RAS mimetic to block downstream signaling cascades including PI3K and RAF*

Highlights

- Rigosertib binds to the RAS-binding domains (RBDs) of multiple RAS effectors
- Binding of rigosertib to RAF-RBD inhibits RAS-RAF interaction and impairs the kinase
- Rigosertib inhibits MEK-ERK pathway activated by growth factors and oncogenic RAS

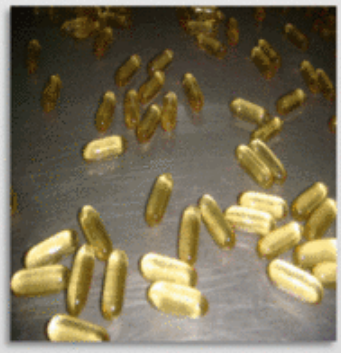


*RAF cascade shown

Two Rigosertib Formulations

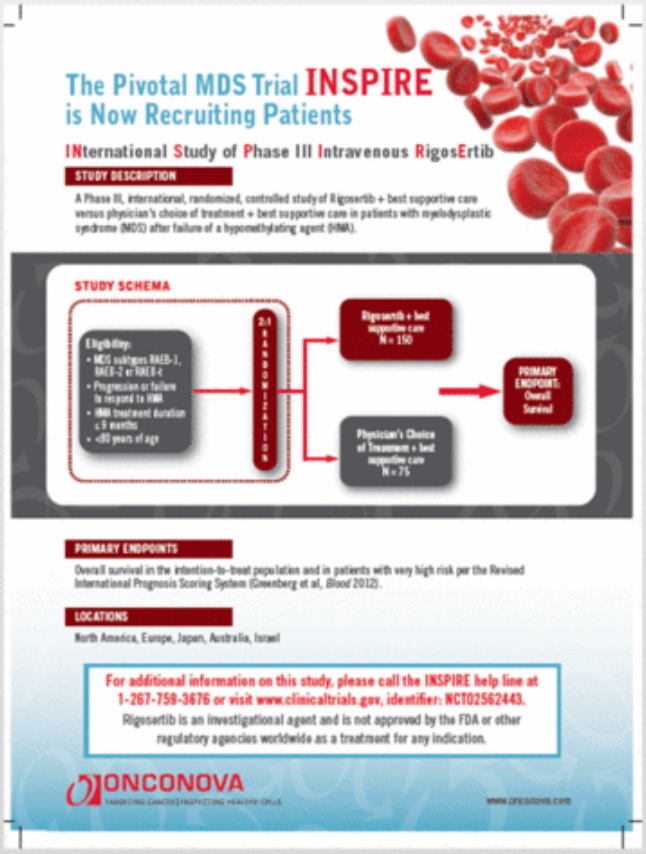
- IV (Phase 3 INSPIRE ongoing)
  - Continuous infusion using a portable pump
  - >500 patients treated in trials
  - Lead indication 2nd-line HR-MDS

- Oral (Phase 2 enrolled)
  - Bioavailability ~35%
  - >200 patients treated
  - Combination with azacitidine for HR-MDS and AML



Composition of matter patent protection plus orphan drug indications

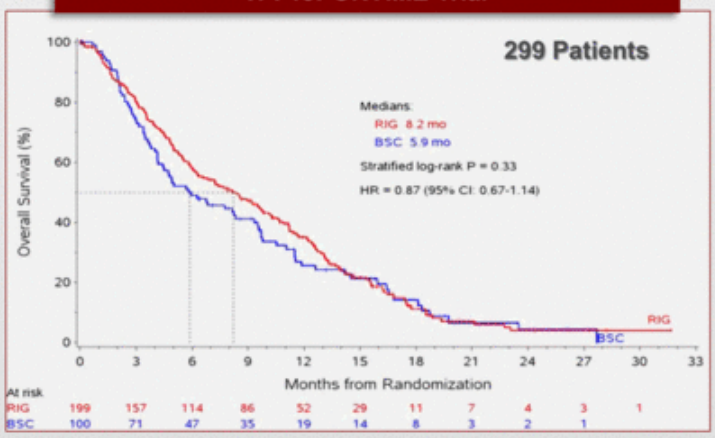
INSPIRE: Rigosertib Phase 3 Trial



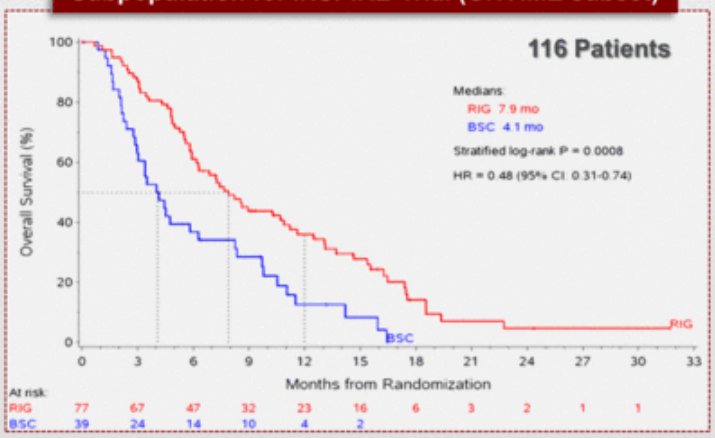
Patient Population for Phase 3 INSPIRE Trial

ONTIME paper* recently published in *Lancet Oncology*

ITT for ONTIME Trial



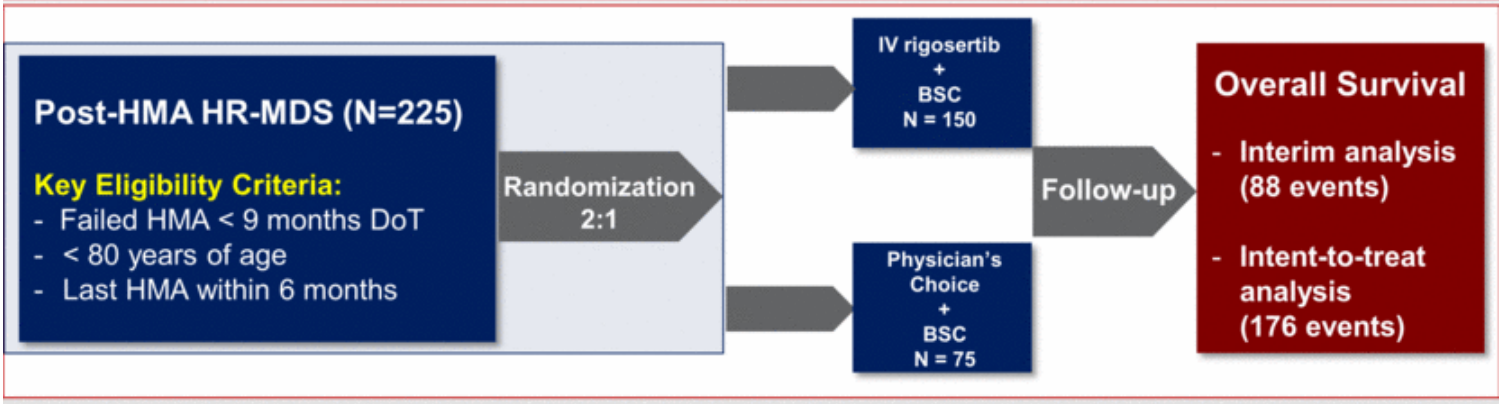
Subpopulation for INSPIRE Trial (ONTIME subset)



- ITT OS analysis of ONTIME
  - HR= 0.87; NS survival benefit
- ITT OS of proposed INSPIRE population
  - HR = 0.48; P = 0.0008

*Rigosertib versus best supportive care for patients with high-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, phase 3 trial
Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, and others
The Lancet Oncology, Vol. 17, No. 4, p496–508
Published online: March 8, 2016

Design of Phase 3 INSPIRE Trial



- **Statistical analysis: two analysis planned**
  1. α for ITT = 0.04; α for IPSS-R VHR = 0.01
  2. Trial can succeed in two ways: ITT population or IPSS-R Very High Risk
- Genomic sequencing of patient samples

Regarding new trials for MDS (Comment)
Novel trial designs for high-risk myelodysplastic syndromes
Emilio P Alessandrino, Matteo G Della Porta
The Lancet Oncology, Vol. 17, No. 4, p410–412
Published online: March 8, 2016

Comparison of Trials

Parameter	ONTIME Trial	INSPIRE Trial
Total patients	299(270[1])	225
Sites	79[2]	Up to 135
Geography	US and EU (6 countries)	U.S., EU, Japan, Israel, Australia
Indication	Post-HMA HR-MDS	Post-HMA HR-MDS
	Key Eligibility Criteria	
Age	No upper limit	**< 80 years**
Duration of HMA therapy	No restriction	**≤ 9 months**
Time after HMA therapy	≤ 24 months	≤ 6 months
	Efficacy Analysis	
Primary endpoint	Overall Survival	Overall survival
Basis for approval	ITT analysis	ITT *or* IPSS-R VHR subgroup
Interim look	No	Yes

[1] Original trial was for 270 patients; over-enrollment driven by site interest and patient need
[2] Most productive site (MD Anderson) provided ~15% of total enrollment; enrolled first patient for INSPIRE

Data Analysis for INSPIRE Trial

Trial to be conducted in 16 countries on 4 continents

- **Primary endpoint is overall survival**
  - Entire trial (ITT) after 176 events have occurred
  - If the ITT analysis is negative, a second analysis of IPSS-R VHR subgroup is permitted
- **Interim analysis planned**
  - ITT analysis after 88 events
  - Types of analysis are being discussed as a part of Statistical Analysis Plan
- **Secondary analysis includes**
  - By region of enrollment (U.S., EU, ROW)
  - Karyotypes

INSPIRE Trial Progress

Goals:

- 16 countries
- 135 sites
- 225 randomized patients

Status:

- 50+ sites Initiated
  - U.S., Europe, Japan
  - Israel, Australia coming up
- Patients enrolled in US and EU
  - 1st patient in Japan expected in Q2-16

Interim analysis planned for H2-2017

**SIV: Site Initiation Visit*

Lancet Oncology Publication

Phase 3 ONTIME trial data in a peer-reviewed journal (March 2016)

Rigosertib versus best supportive care for patients with high-risk myelodysplastic syndromes after failure of hypomethylating drugs (ONTIME): a randomised, controlled, phase 3 trial

*Guillermo Garcia-Manero, Pierre Fenaux, Aref Al-Kali, Maria R Baer, Mikkael A Sekeres, Gail J Roboz, Gianluca Gaidano, Bart L Scott, Peter Greenberg, Uwe Platzbecker, David P Steensma, Suman Kambhampati, Karl-Anton Kreuzer, Lucy A Godley, Ehab Atallah, Robert Collins Jr, Hagop Kantarjian, Elias Jabbour, Francois E Wilhelm, Nozar Azarnia, Lewis R Silverman, for the ONTIME study investigators**

www.thelancet.com/oncology Published online March 8, 2016 http://dx.doi.org/10.1016/S1470-2045(16)00009-7

Rigosertib + Azacitidine Phase 2 Trial public

Why combination therapy?

Nature Reviews Clinical Oncology (2005)

Combination therapy with DNA methyltransferase inhibitors in hematologic malignancies

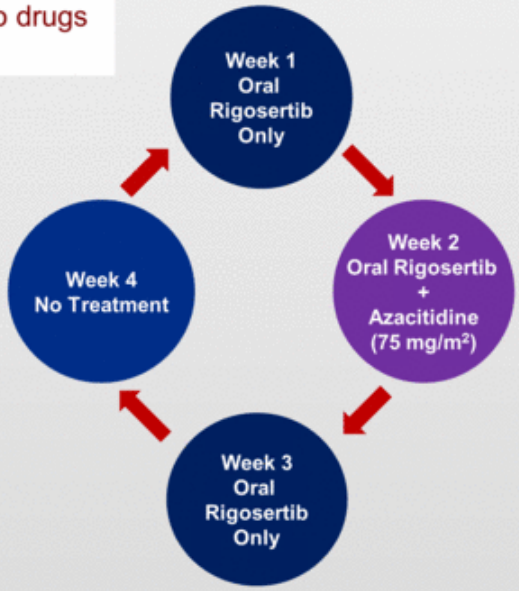
Steven D Gore

A variety of epigenetic changes contribute to transcriptional dysregulation in myelodysplastic syndromes (MDSs) and acute myeloid leukemia (AML). DNA methyltransferase (DNMT) inhibitors—azacitidine and decitabine—have significant activity in the treatment of MDS. Despite marked activity in myeloid malignancy, ***monotherapy with DNMT inhibitors is limited by low complete and partial response rates (7–20%) and median response durations of 15 months***. As with classical cytotoxic therapy, the targeting of biologic pathways and mechanisms **may best be accomplished using a combination of agents offering complementary mechanisms and synergistic pharmacodynamic interactions**. The goal of this approach is to improve response rates, quality, and duration, and to minimize adverse events.

Rigosertib + Azacitidine Combination Therapy

- Based on synergistic activity between rigosertib and azacitidine (US Patent)
  - Activity dependent on the sequence of administration of the two drugs
  - Two distinct mechanisms of action combined

- Phase 1 combination was well tolerated with evidence of efficacy in patients with MDS*
- Azacitidine given one week per month (full dose and administrative scheme per label)
- Rigosertib given 3 of 4 weeks (at recommended Phase 2 dosing of 560/280 mg BID)
- Adverse event profile of combination similar to single-agent azacitidine (per label)



** Navada S, Garcia-Manero G, Wilhelm F, et al. A phase I/II study of the combination of oral rigosertib and azacitidine in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML). ASH 2014; Abstract 3252.*

Rigosertib + Azacitidine Combination: Phase 2 Data

- **Overall response rate of 84% in 19 patients who never received an HMA**
- Overall response rate of 64% in 11 patients who received prior HMA
- HMA naïve and HMA failure patients received same dose/schedule of treatment with combination

Response Assessment per 2006 IWG Criteria			
	All (n=30)	HMA Naïve/1st-line (n=19)	HMA Failure*/2nd-line (n=11)
Complete Remission	6/30 (20%)	5/19 (26%)	1/11 (9%)
Overall Response Rate	23/30 (77%)	**16/19 (84%)**	7/11 (64%)

*8 patients received previous therapy with azacitidine, 2 with decitabine and 1 with both HMAs; prior HMA cycles ranged from 4-20

** Navada S, et al. A phase 2 study of the combination of oral rigosertib and azacitidine in patients with myelodysplastic syndrome (MDS). ASH 2015; Abstract 910.*

Intellectual Property Summary

- Onconova portfolio contains only New Chemical Entities
  - All NCEs are patent protected for composition of matter and other claims
- Rigosertib (ON 01910.Na) covered by issued US and other patents
  - Earliest to expire composition claim valid until 2026
  - Potential for Hatch-Waxman extensions
  - Composition of rigosertib combination with azacitidine expires 2028
  - Single digit royalty to Temple University
- Orphan designation granted in US, Europe and Japan for rigosertib in MDS
- Issued US and other patents cover the rest of the pipeline
  - Briciclib, Recilisib are in in Phase 1
  - ON 123300 (ARK5+CDK4/6 inhibitor) in advanced preclinical stage

Milestones and Goals

Program Title	2016
2nd-line HR-MDS (rigosertib IV)	☑ ONTIME publication in *Lancet Oncology* ☑ Patient enrollment in European sites ❑ Patient enrollment in Japanese sites ❑ Data release from single-arm Phase 3 trial (04-24)
Combination for MDS/AML (oral rigosertib + AZA)	❑ Complete results (updated response and IPSS-R analysis and duration of response) from Phase 2 trial ❑ End of Phase 2 meetings with FDA and overseas ❑ Initiate next stage of development
Other Highlights	☑ Publication of mechanism of action studies in high-profile scientific journal, *Cell* ❑ Business development transactions for early-stage pipeline

Key 2017 goals: Interim analysis of INSPIRE; next stage of development of combination therapy

Summary

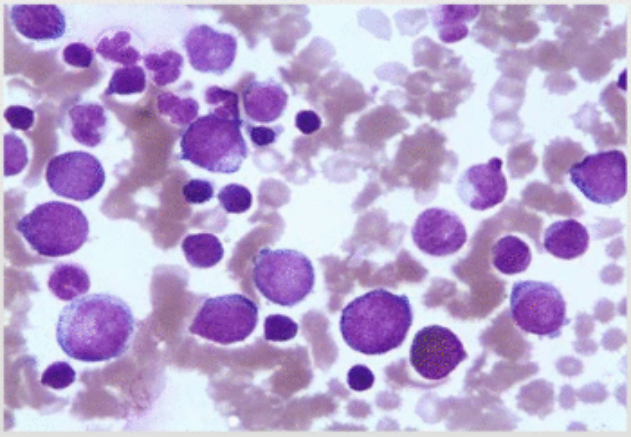
- **Large opportunity: unmet medical need in MDS**
  - Last approval for MDS more than a decade ago
  - IV + oral rigosertib products have large potential value
- **Key milestones and upcoming inflection points**
  - Phase 3 interim analysis 2017; Top-line data 2018
  - Combination Phase 2 data to be reviewed with FDA in H2-16
- **Established Co. with a differentiated late-stage product**
  - Current funds sufficient for 2016
  - Pursuing business development opportunities

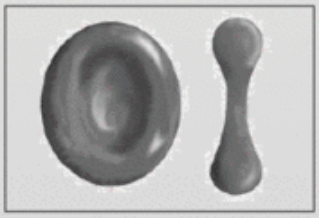
ONCONOVA THERAPEUTICS

Back-up Slides

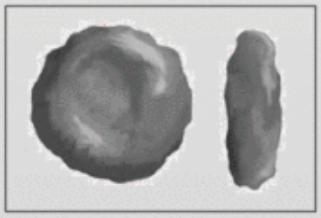
What is MDS?

Microscopic View of MDS Bone Marrow





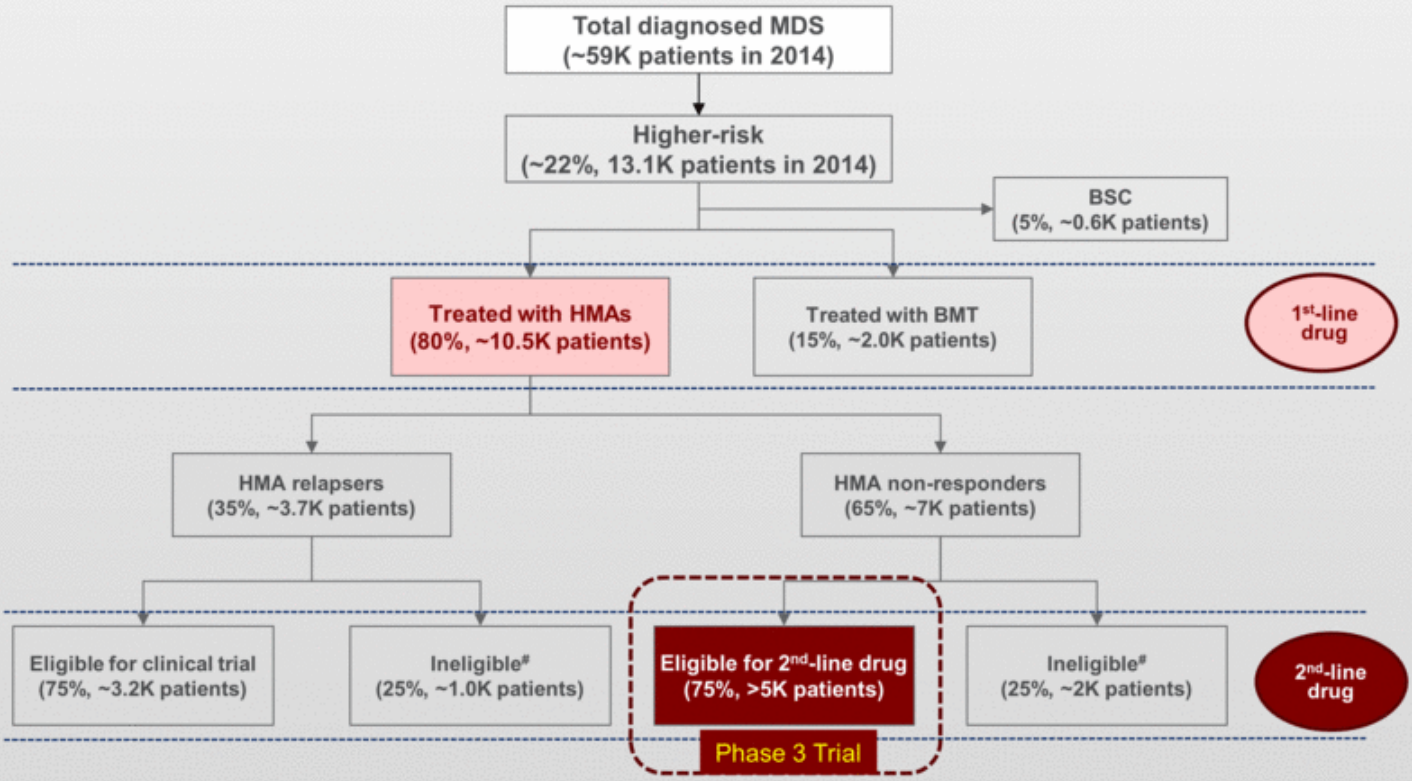
Healthy, mature red blood cells



Abnormal or "dysplastic" red blood cells

- **Definition**: Bone marrow insufficiency of one or more circulating blood cells, with 5%-30% immature blast (leukemic type) cells in the bone marrow
- **Major Problems:** Bleeding, infections, iron overload from multiple red blood cell transfusions
- **Cause**: Possible causes include chemicals and radiation, or previous chemotherapy treatment; associated with various acquired chromosomal and genetic abnormalities

Rigosertib in Higher-risk MDS



Refuse or medically ineligible for additional Tx with currently available therapies and are treated with supportive care or hospice care

Advisory Board

Ross C. Donehower, M.D.	Johns Hopkins Sidney Kimmel Comprehensive Cancer Center
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Stephen Nimer, M.D.	Sylvester Cancer Center at the University of Miami Hospitals and Clinics
David R. Parkinson, M.D.	CEO, ESSA Pharmaceuticals, previously Venture Partner at NEA
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