ONCONOVA THERAPEUTICS

Corporate Presentation

Sachs 16th Annual Biotech in Europe Forum
for Global Partnering and Investment

September 27-28, 2016

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
- IPO in 2013: NASDAQ Ticker ONTX
- Focused on unmet needs in Myelodysplastic Syndromes (MDS*)
  - Lead compound rigosertib
  - IV rigosertib in global Phase 3 trial
  - Oral rigosertib completed enrollment of Phase 2 trial
- Funded to deliver multiple Phase 3 milestones in 2017
  - $27.6 million as of 7/31/2016

**MDS: A disease of the elderly, affecting bone marrow function; patients can progress to acute myeloid leukemia (AML)*

Onconova Product Pipeline

Program	Partnership	Indication	Preclinical	Phase 1	Phase 2	Phase 3	NDA/MAA
Single-agent IV rigosertib	***Partnered with SymBio in Japan/Korea****	**2nd-line Higher-risk (HR-MDS)**	**INSPIRE Pivotal Trial; interim analysis expected in 2017**				**Key Focus**
Oral rigosertib + azacitidine		**1st-line Higher-risk (HR-MDS)**	**End of Phase 2 Meeting with FDA conducted**				
IV Briciclib		**Solid tumors**	**Dose-escalation Phase 1 Trial****			**eIF4E targeting**	
Recilisib	***Global & regional partnership opportunities***	**ARS*****	**Non-Human Primate Efficacy** *Supported by U.S. Government funds*			**Targets radiation-induced apoptosis**	
ON 123300		**CDK4/6 overactive tumors**	**Pre-IND Stage**			**ARK5+CDK4/6 Targeting**	

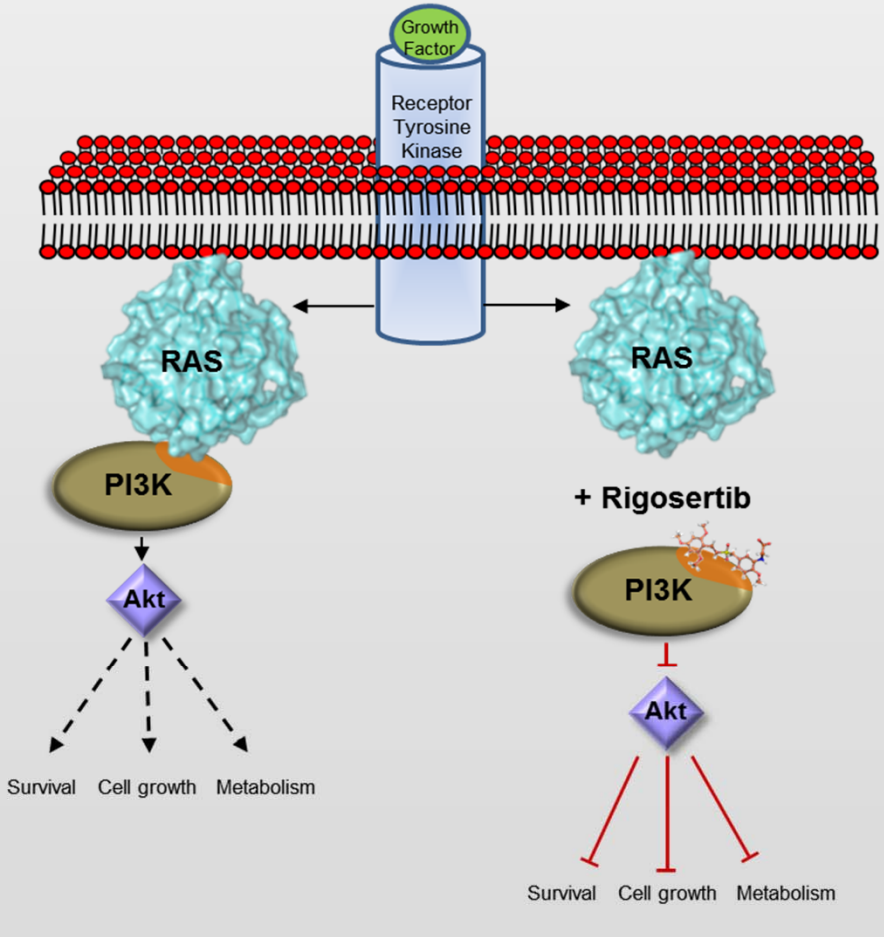
**Onconova retains rights elsewhere, including USA*
***Trial on hold pending manufacturing of new product lot; ***Acute Radiation Syndrome*

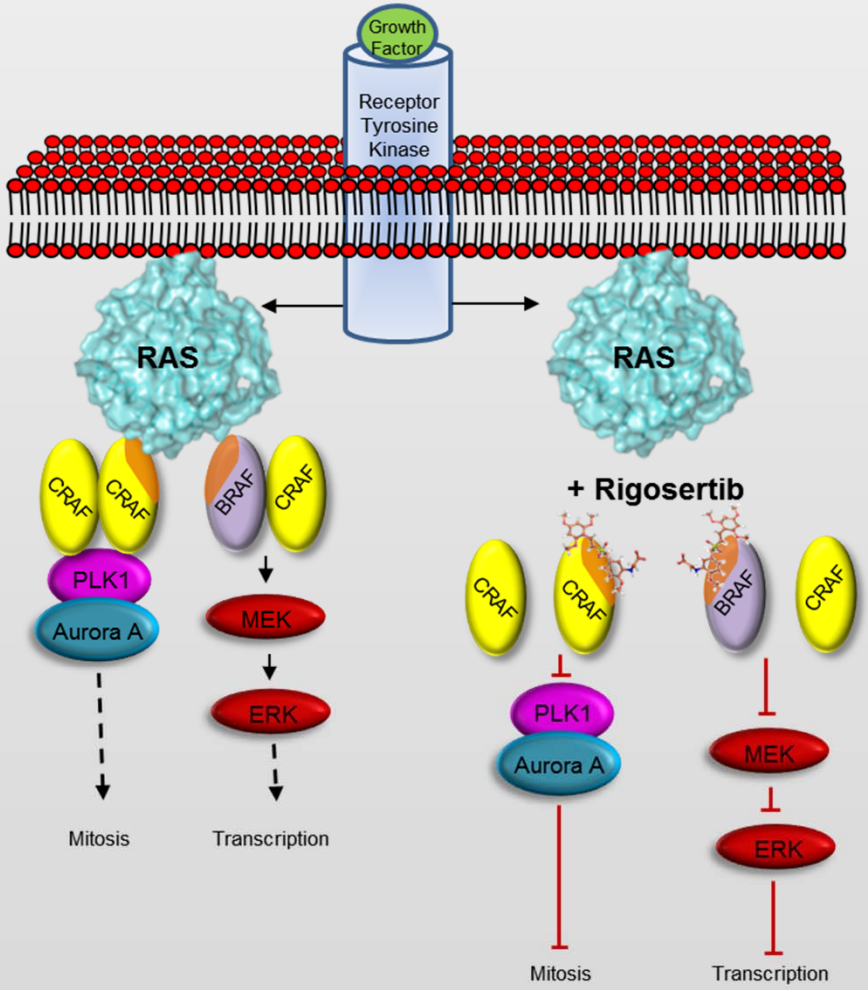
Rigosertib Overview

- Patent protected through 2026 (composition), and 2028 (combination)
  - Orphan drug designation granted in U.S., EU and Japan
  - Novel mechanism of action directed against RAS pathways
- Phase 3 INSPIRE trial enrolling higher-risk MDS (HR-MDS) patients
  - Pre-planned interim analysis in H2-2017
  - Top-line data expected in 2018
- Phase 2 oral rigosertib + azacitidine trial completed enrollment
  - End-of-Phase 2 meeting with FDA targeted for H2-2016
- Rigosertib has extensive clinical trial database
  - Safety data from more than 1,000 patients (IV and oral drug)

Novel Mechanism of Action

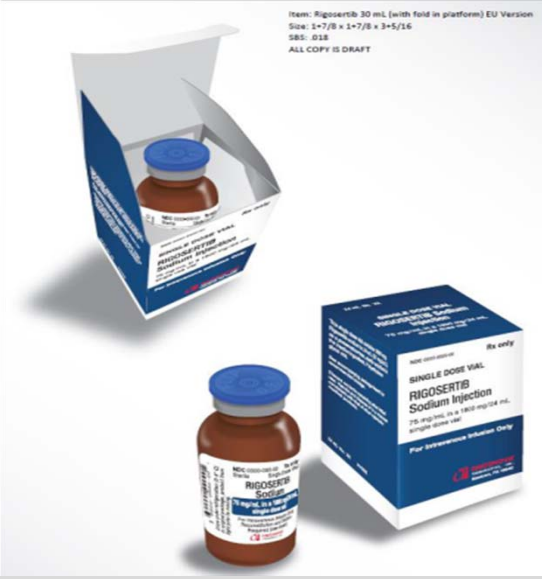
Rigosertib acts as RAS mimetic to block downstream signaling cascades including PI3K and RAF





Two Rigosertib Formulations

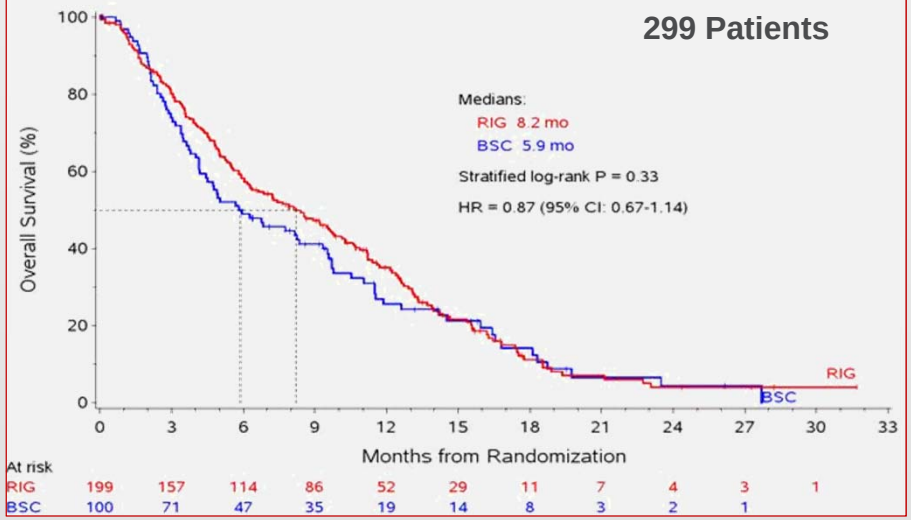
- IV (Phase 3 INSPIRE ongoing)
  - Continuous infusion using a portable pump
  - >500 patients treated in trials
  - Lead indication 2nd-line HR-MDS
- Oral (Phase 2 enrolled)
  - Bioavailability ~35%
  - >200 patients treated
  - Combination with azacitidine for HR-MDS and AML



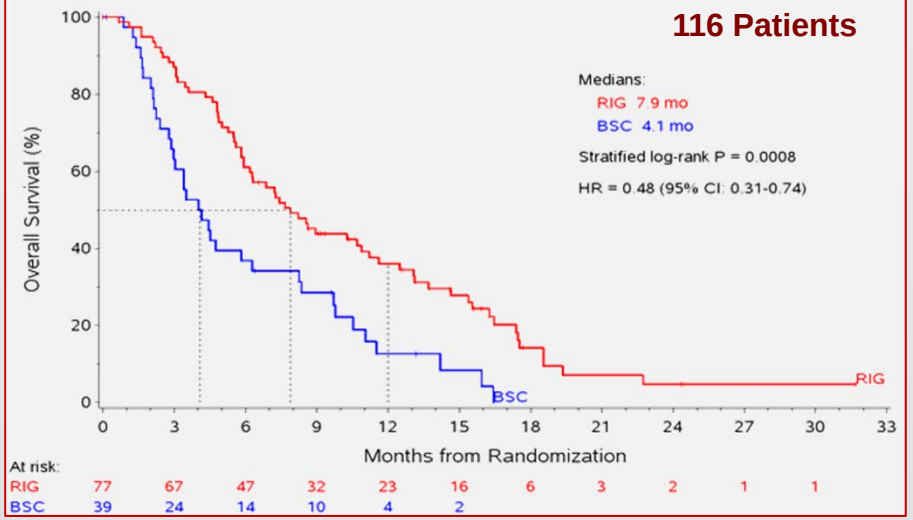
Patient Population for Phase 3 INSPIRE Trial

Data from ONTIME paper* published in *Lancet Oncology*

ITT for ONTIME Trial



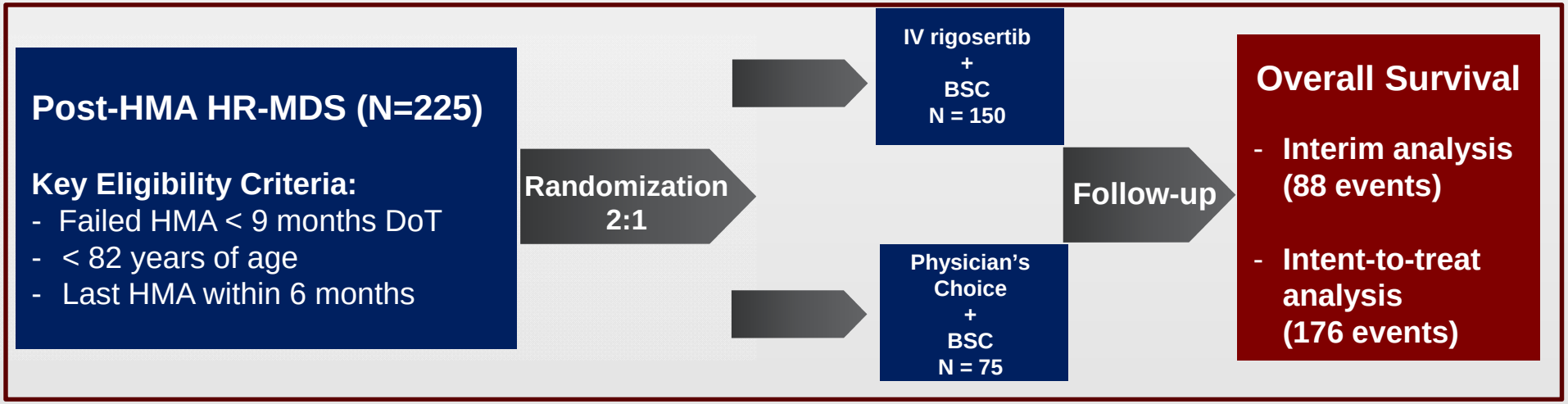
Subpopulation for INSPIRE Trial (ONTIME subset)



- ITT Overall Survival analysis of ONTIME, median 2.3 months
  - HR= 0.87; Non significant survival benefit
- ITT OS of proposed INSPIRE population, median 4.8 months
  - HR = 0.48; 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

INSPIRE: Global Phase 3 Trial

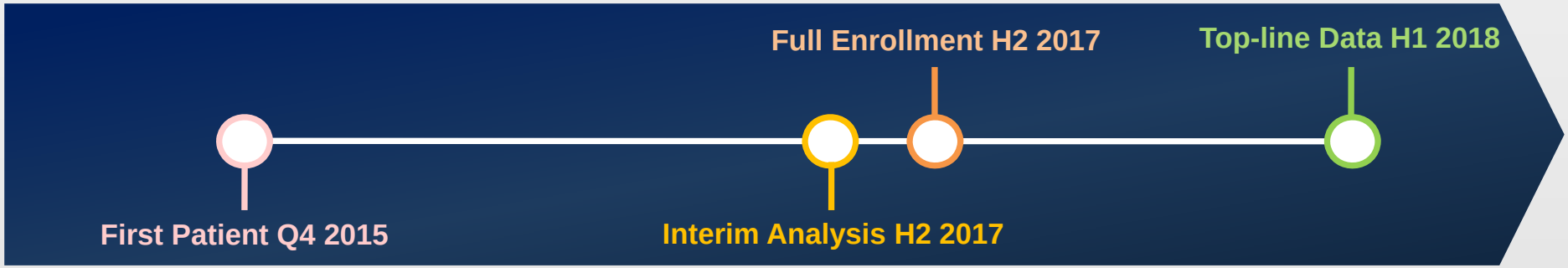


- Statistical analysis: two analyses planned
  - Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
  - α for ITT = 0.04; α for IPSS-R VHR = 0.01
    - Trial can succeed in two ways: ITT population or IPSS-R Very High Risk
- Genomic sequencing of patient samples

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

Data Analysis for INSPIRE Trial

Timeline for Global Trial Conducted on Four Continents



- Primary endpoint is overall survival
  - Entire trial (ITT analysis) 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 in discussion as a part of Statistical Analysis Plan
- Secondary analysis includes
  - By region of enrollment (U.S., EU, ROW)
  - Karyotypes; genomics

Oral Rigosertib + Azacitidine for 1st-line MDS

In higher-risk MDS patients:

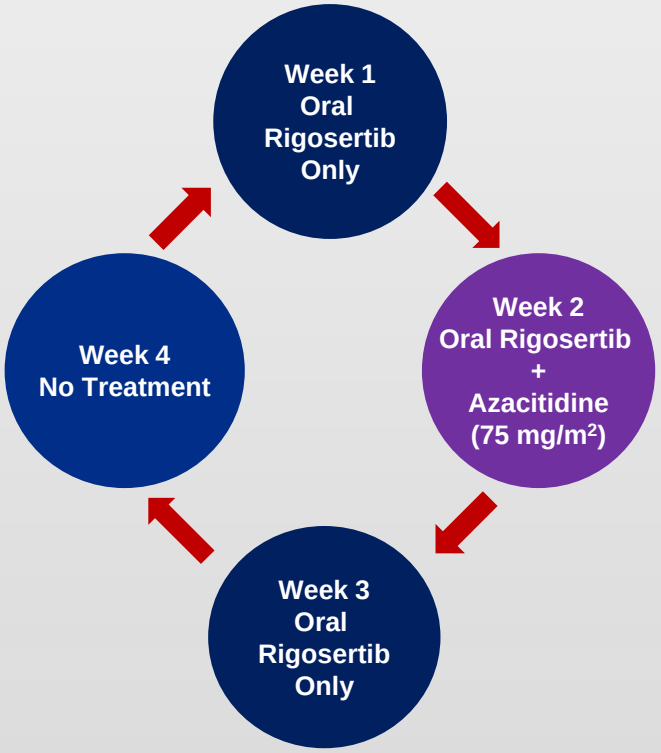
- Efficacy of single-agent DNMT* inhibitors (HMAs) is limited
  - Low CR and PR rates (7-20%)
  - Limited median duration of benefit of ~15 months
- Combination with other agents is warranted
  - Combinations should not add burdensome toxicities
- DNMT inhibition in combination with novel mechanisms may improve response rates and duration of benefit

**DNA Methyl Transferase inhibitors are also known as Hypomethylating Agents (HMAs)*

Rigosertib + Azacitidine Combination

Rigosertib and Azacitidine administered in sequence

- Phase 1 combination was well tolerated
  - 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
  - Recommended Phase 2 dose 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.

Phase 2 Rigosertib + Azacitidine

Interim 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			
Patient Characteristics	All (n=30)	HMA Naïve/1st-line (n=19)	HMA Failure*/2nd-line (n=11)
Complete Remission (CR %)	6/30 (20)	5/19 (26)	1/11 (9)
Overall Response Rate (ORR %)	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

Pipeline Beyond Rigosertib

IV Briciclib	*Seeking Partners**	Solid tumors	Dose escalation Phase 1 trial*	eIF4E targeting
Recilisib	*Seeking Partners**	ARS***	Non-Human Primate Efficacy *Supported by U.S. Government funds*	Targets radiation-induced apoptosis
ON 123300	*Seeking Partners**	CDK4/6 overactive tumors	Pre-IND Stage	ARK5+CDK4/6 Targeting

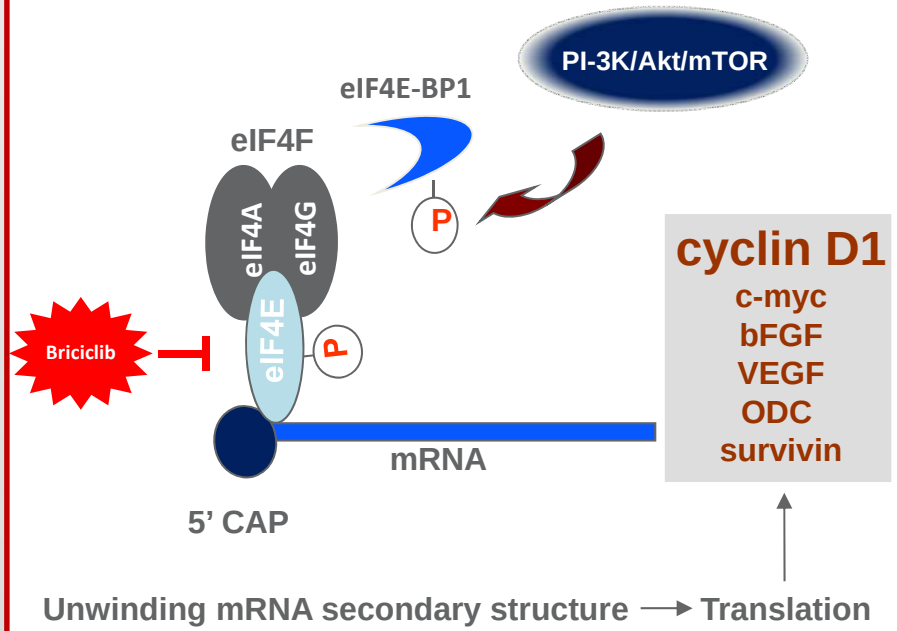
**Onconova is seeking regional and worldwide partnerships*
***Trial on hold pending manufacturing of new product lot;*
****Acute Radiation Syndrome*

- Onconova portfolio contains New Chemical Entities
  - All NCEs are patent protected for composition of matter and other claims
- Issued U.S. and other patents coverage
  - Briciclib and recilisib are in in Phase 1
  - ON 123300 (ARK5+CDK4/6 inhibitor) in advanced preclinical stage

Briciclib Molecular Mechanism of Action: eIF4E Binding

- eIF4E in cancer
  - Expression elevated in 30% of cancers
  - Increased expression associated with poor prognosis
- Briciclib binds to eIF4E to inhibit cap-dependent translation initiation
- Cap-dependent process critical for:
  - Proliferation (cyclin D1)
  - Angiogenesis (VEGF)
  - Survival (survivin)
- Briciclib may induce tumor cell death by inhibiting translation initiation mechanism

Briciclib mechanism of action involves disruption of eIF4E-mediated translation



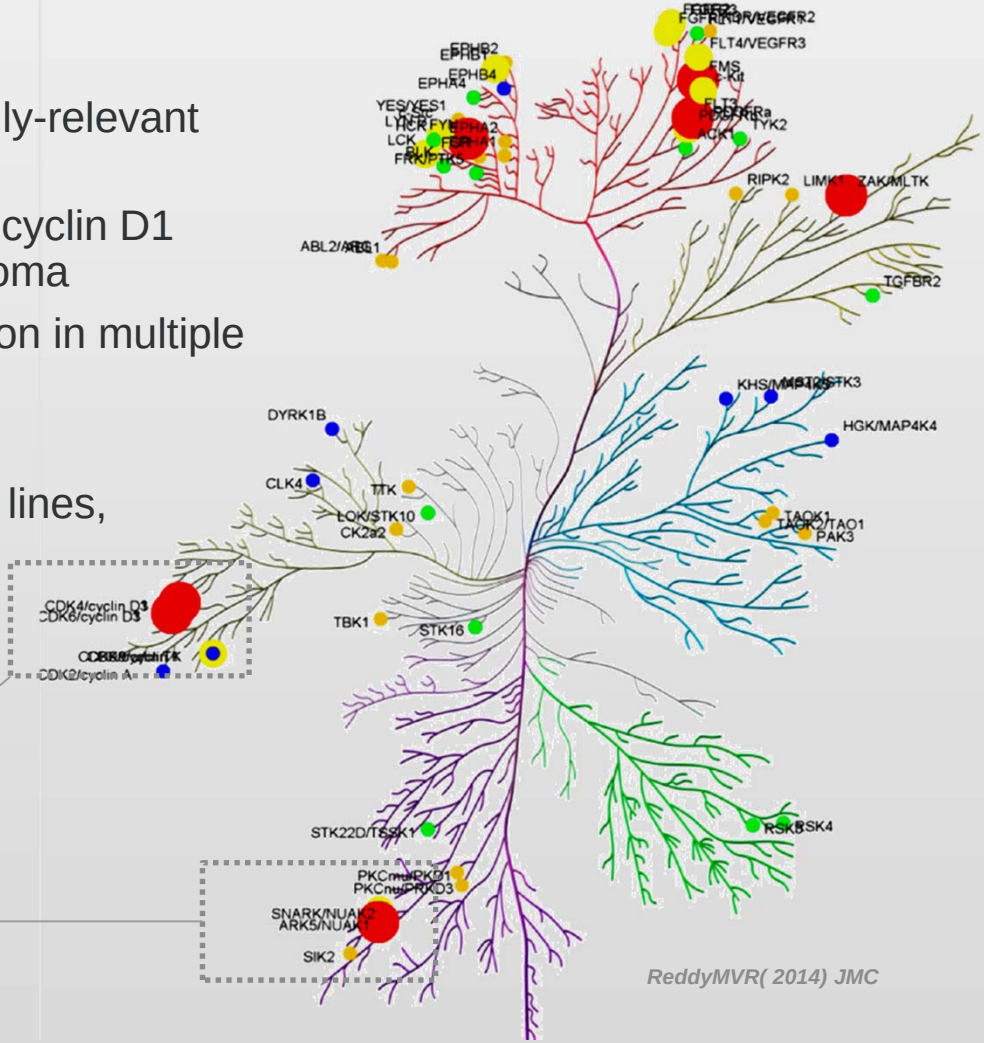
Briciclib Overview

- Phase 1 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 potential indications
  - Certain solid tumors
  - MCL and other lymphomas
  - Single agent and combination therapy

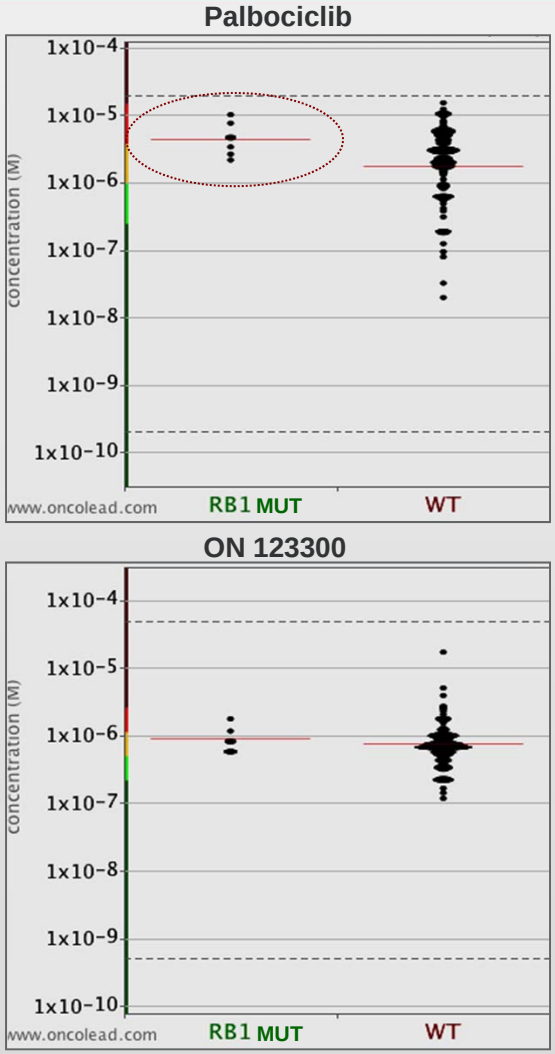
ON 123300: Differentiated CDK4/6 and ARK5 Inhibitor

- Composition of matter patent until 2031
- Nanomolar potency against therapeutically-relevant kinase targets:
  - CDK4/6 – aberrant activation due to cyclin D1 overexpression in mantle cell lymphoma
  - ARK5 – supports c-MYC dysregulation in multiple myeloma
- Single-agent activity in MCL and MM cell lines, primary patient samples and xenografts

Kinase	ON 123300
CDK4/D1	3.87
CDK6/D1	9.82
ARK5	4.95



Differentiated Cytotoxic Activity



Cytotoxicity Screening_Oncolead

- Single-agent activity of pure CDK4/6 inhibitors, like palbociclib, is diminished in cells lacking G1 checkpoint
- **ON 123300 is cytotoxic in G1 checkpoint disabled (Rb mutant) cells due to targeting of other kinases**
- Additional targets yield broader single-agent cytotoxicity compared to pure CDK4/6 inhibitors

Key Milestones Ahead

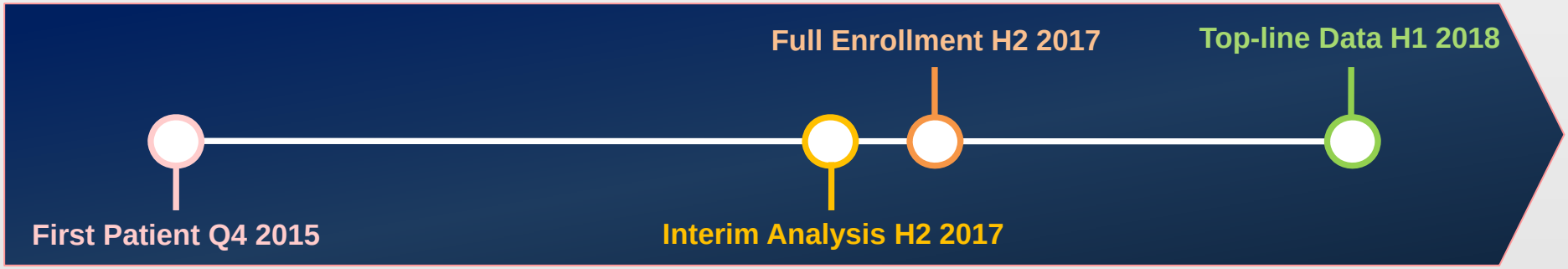
Program	Milestones and Goals
INSPIRE trial in 2nd-line MDS	❑ Activate all INSPIRE trial sites on four continents ❑ Enrollment update
Combination Therapy (Oral rigosertib + Azacitidine)	❑ Scientific presentation of Phase 2 Data ❑ End of Phase 2 meetings with FDA and overseas ❑ Pivotal trial design (Q4-16 or Q1-17)
Other	❑ Potential business development transaction(s)

Key 2017 goals

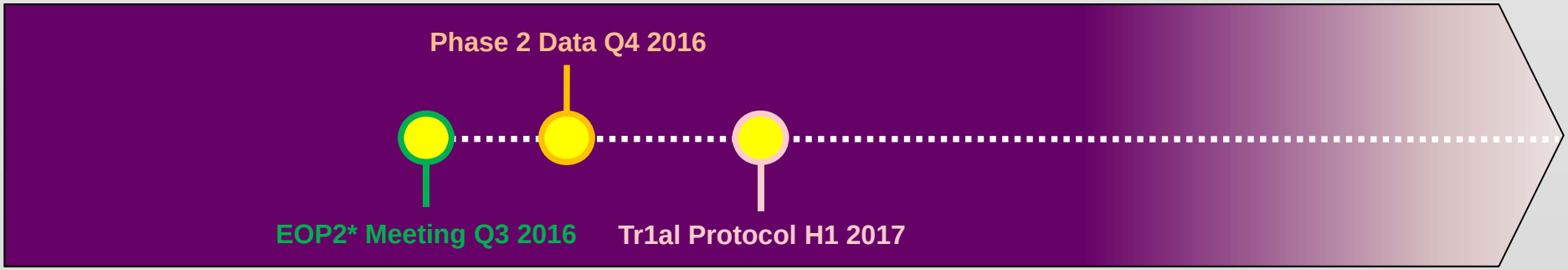
- Initiate pivotal trial with oral rigosertib combination therapy
- Interim analysis of INSPIRE trial
- Full enrollment of INSPIRE trial

Pivotal Trial Timelines

Timeline for INSPIRE Global Trial



Timeline for Development of Oral Rigosertib + Azacitidine



*EOP2: End of Phase 2 meeting

Upcoming Presentations and Conferences

October 17	ONTX sponsored KOL Analyst/Investor event on RAS as a therapeutic target, NYC
October 18-19	BIO Investor forum, San Francisco*
October 26-28	BIO Latin America, Sao Paolo, Brazil*
November 7-9	**BIO Europe, Cologne, Germany***
December 3-6	ASH conference, San Diego
**Anticipated*	

Summary

- **Large opportunity: unmet medical need in MDS**
  - Last new drug for MDS approved more than a decade ago
  - IV + oral rigosertib differentiated products with significant potential value
  - RAS pathway mechanism opens doors to additional indications
- **Key milestones and upcoming inflection points**
  - Combination Phase 2 data to be reviewed with FDA in H2-16
  - Phase 3 interim analysis 2017; top-line data 2018
- **Strong financial profile**
  - Current funds sufficient to take the Company through 2017 milestones
  - Business development opportunities with rigosertib and pipeline