ONCONOVA THERAPEUTICS

Corporate Update

June 2018 | Nasdaq: ONTX

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.

PORTFOLIO: RIGOSERTIB AND OTHER OPPORTUNITIES

Lead

- Phase 3 INSPIRE trial progressing to completion after promising interim analysis and enhanced powering
- Trial completion projected in H1-2019

Oral

- Oral rigosertib provides two large-market opportunities
- Combination trial for front-line high risk MDS ready to advance to Phase 3 in H2-2018

More

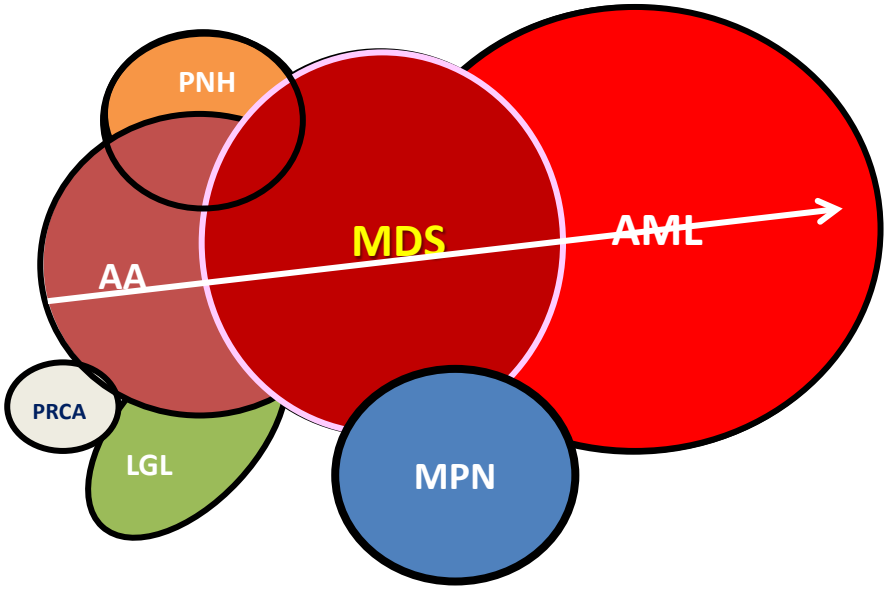
- NCI funded RASopathies trial for rare pediatric indications
- New CDK inhibitor presents opportunities for the future

ONCONOVA THERAPEUTICS, INC.

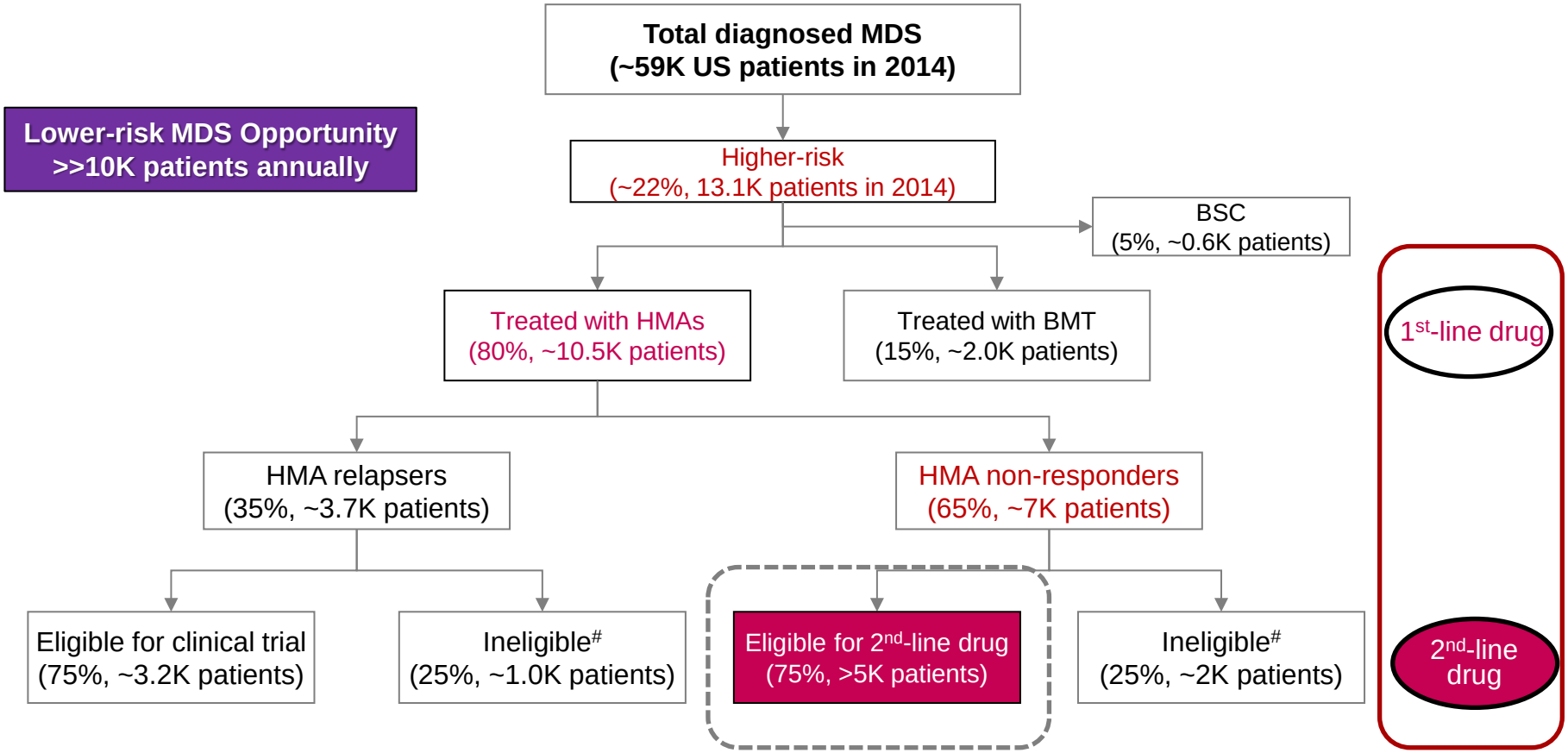
- Founded in 1998; IPO in 2013 (Nasdaq: ONTX)
- Phase 3 stage clinical candidate: rigosertib
  - Targets RAS effector pathways (Cell, 2016)
  - Focused on Myelodysplastic Syndromes (MDS)
- Rigosertib partnered in Japan and Latin America
  - Additional partnerships to come
- Broad pipeline of drug candidates
  - Larger opportunities in solid tumors and other indications

MDS IS RELATED TO OTHER BONE MARROW DISEASES

- MDS: malignant bone marrow disorder characterized by:
  - Bone marrow failure leading to low blood counts
  - 30% of patients progress to AML
- 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
  - New therapy could have $billions opportunity



RIGOSERTIB IN MYELODYSPLASTIC SYNDROMES



- Rigosertib for 2nd-line patients (INSPIRE Phase 3 trial)
- For 1st-line patients, in combination with Azacitidine, the current standard of care
- Oral rigosertib for transfusion dependent lower-risk patients

RIGOSERTIB CLINICAL STAGE PROGRAMS

Disease	Formulation	Indication	Stage	Expected Timelines	Potential Market Opportunity (US)/Benefit	
MDS*	Intravenous	HR-2nd line. No approved product following HMA failure	Phase 3	• Interim analysis completed • Phase 3 completion 2019	~5,000 patients	No directly competing FDA approved product in the market
	Oral	HR-1st line In combination with AZA	Phase 2	Phase 3 protocol, SPA process, in 2018	~18,000	No oral NCE approved since 2005
	Oral	Lower Risk	Phase 2	Select patient population in 2018	>10,000	Longer potential duration of treatment
RASopathies^	Intravenous and oral	JMML/other Ras Pathway diseases	Phase 1	• NIH CRADA signed • Proof of concept in 2019	Rare disease	Pediatric clinical trial

IV product for infusion

Oral soft gel capsules

**Myelodysplastic Syndromes (MDS) are bone marrow diseases related to failure of cellular production and possible transformation to acute leukemia (MSKCC website, other academic resources.)*

^RASopathies are rare inherited diseases of children that include cancer and cardiovascular disease (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4115674/pdf/nihms604870.pdf)

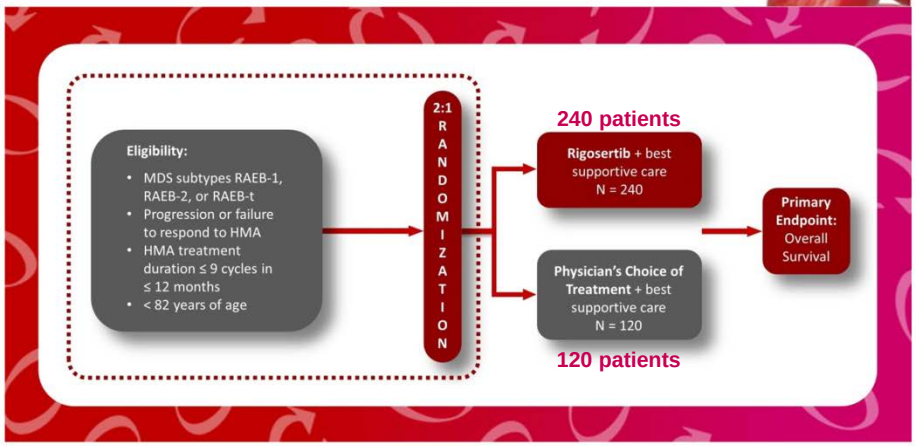
INSPIRE PHASE 3 TRIAL RESULTS EXPECTED IN 2019

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

INternational **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" signal

Top-line Data
H1-2019 (projected)

- **Interim analysis was conducted after 88 events: January 2018**
- **Topline data after 288 events expected in H1-2019**
- **Trial running at ~170 sites in 22 countries on 4 continents**

INTERIM ANALYSIS

- Adaptive trial design implemented after DMC meeting
  - Sample size re-estimation per approved Statistical Analysis Plan (SAP)
    - 135 patients to be added to enhance the power of trial
- Top-line analysis to be performed after 288 events
  - Two successive survival analysis permitted by SAP
    - ITT P value target 0.039; Very High Risk (VHR) subgroup P value target 0.01

Key changes in INSPIRE trial after interim analysis

- Increased power of trial with 135 patients added
  - Greater proportion of Very High Risk patients in the ITT group
- Higher potential probability of success with two successive analysis
  - Trial directed to the highest unmet medical need in MDS

FACTORS INFLUENCING INSPIRE TRIAL AND TOP-LINE DATA

- Interim Analysis promising results may spur interest in the trial
  - Enrollment rate may increase
  - Potential for patient advocacy support

- High proportion of VHR subgroup in the trial enrolled so far
  - ONTIME trial had 43% of the patients in the VHR subgroup
  - INSPIRE eligibility criteria informed by ONTIME results

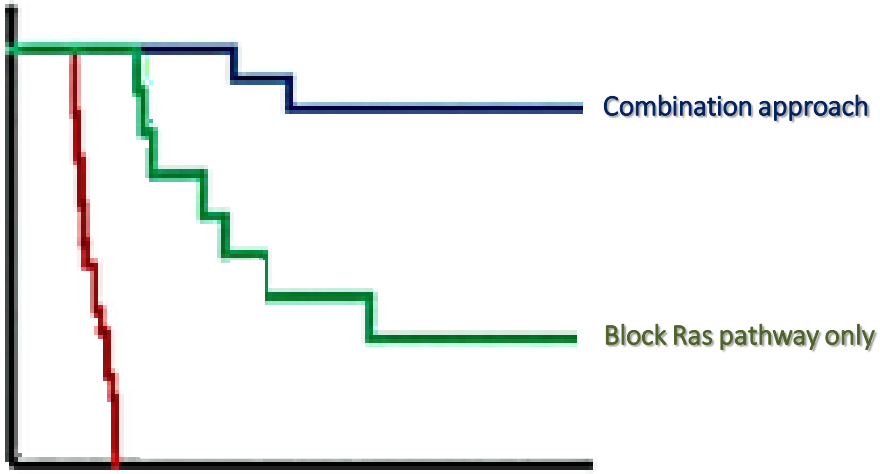
- INSPIRE trial is directed to a significant unmet medical need in MDS
  - Currently no other program is believed to be in advanced trials

MECHANISTIC RATIONALE FOR COMBINATION THERAPY WITH RIGOSERTIB + AZACITIDINE

Preclinical evidence supports synergism of rigosertib + azacitidine combination

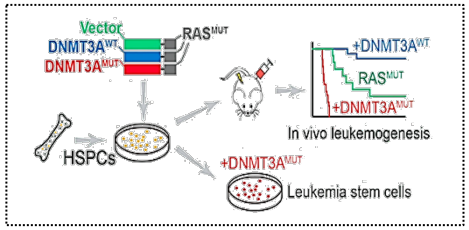
AML Animal Model

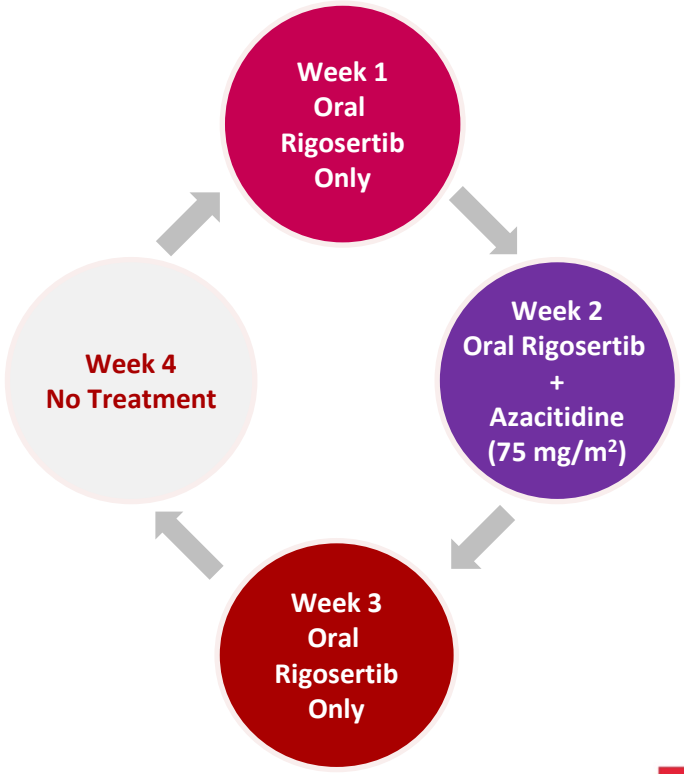
Validation of combination approach



Block methylation only

Lu et al., 2016 *Cancer Cell*





More than 80 patients enrolled in combination trial including expansion cohort

RESPONSE DATA FOR ONGOING COMBINATION TRIAL

An additional ~40 patients are currently being enrolled in the expanded Phase 2 trial

Response Criteria	Response per IWG 2006		
	Overall evaluable (N=33)	**No prior HMA (N=20)**	HMA resistant (N=13)
Complete Remission*	**8 (24%)**	**7 (35%)**	**1 (8%)**
Marrow CR + Hematologic Improvement (HI)	10 (30%)	6 (30%)	4 (31%)
Marrow CR alone	6 (18%)	3 (15%)	3 (23%)
Hematologic Improvement alone	1 (3%)	1 (5%)	0
Stable Disease	8 (24%)	3 (15%)	5 (38%)
Overall IWG Response	**25 (76%)**	**17 (85%)**	**8 (62%)**
Clinical Benefit Response	19 (58%)	14 (70%)	5 (38%)

*All responders had CR and no PR was noted in this study

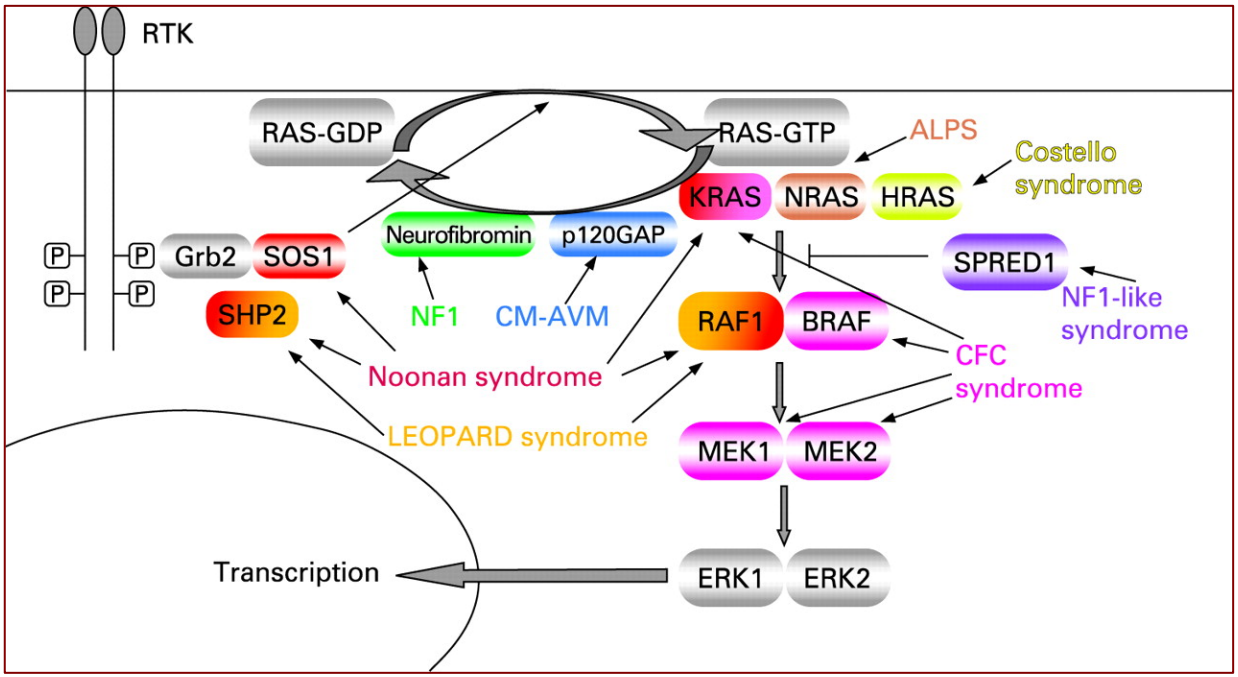
COMBINATION THERAPY: NEXT STEPS AND TIMELINES

Step	Start	Complete	Remarks
Phase 2 expansion *Fully enrolled*	Q1-2017	Q1-2018	▪ Incidence of hematuria reduced (to date in the trial) ▪ Dose and schedule of 1120 mg daily dose to be explored* ▪ Efficacy assessment underway
Phase 3 protocol	Q1-2018	H2-2018	▪ Synopsis created ▪ SPA and BTD submissions contemplated after complete efficacy assessment
Phase 3 trial	Q4-2018	Q2-2020	▪ Rapid enrollment expected ▪ All patients to receive active therapy ▪ Global trial including developing countries ▪ Response endpoint can be achieved in <6-9 months after patient is enrolled

**Dose justification based on safety data from expansion trial and the recently presented oral rigosertib data in Lower-Risk MDS (ASH 2017)*

RASOPATHIES: RIGOSERTIB FOR RARE PEDIATRIC DISEASES

- *Rigosertib mechanism of action mandates exploration in RAS mediated cancers*
- *NCI funded clinical trial permits broad exploration in many Ras pathway diseases*
  - *Provides Pediatric Investigative Plan (PIP) for NDA filing for MDS*
- *Potential JMML program with UCSF could provide independent approval pathway*



Milestones

- NCI CRADA signed January 2018
- NCI Clinical trial IRB review in Process
- Potential for first patient in 2018
- UCSF non-clinical program initiated
  - Funded by LLS
- JMML clinical program could initiate in 2019

NEW PROGRAM: NEXT GENERATION CDK INHIBITOR

Current generation CDK inhibitors

- Recently launched IBRANCE® (Palbociclib, Pfizer), Kisquali® (Ribociclib, Novartis) and Verzenio® (Abemaciclib, Lilly) have been considered to be potential breakthroughs in cancer therapy
  - First FDA approval for CDK 4/6 inhibitor in breast cancer
- ON 123300 differentiated features
  - In addition to CDK4/6 also targets ARK5 controlling cellular metabolism and survival
  - Potential to act as single agent
  - Differentiated pre-clinical effect
  - Blood-brain barrier penetrating properties

Partnership with HanX

- Announced December 19, 2017
- License for Greater China
  - Onconova retains ROW rights
- HanX to fund IND-enabling studies
  - HanX to file in China
  - Onconova to file in US
- Upfront, milestones, royalties
- HanX a specialty Oncology company
  - Phase 1 stage PD-1 antibody
  - Checkpoint blockade and CDK inhibition believed to be synergistic
- Recently completed the pre-IND consultation with the FDA
  - Provided guidance for the manufacturing of ON 123300
  - Confirmed pre-clinical development plan for the submission of an IND application
- Next Milestone is IND

RECENT KEY EVENTS

Year	Date	Advance
2018	May 2	**Closing of Underwritten Public Offering**
	March 5	**License Agreement with Pint Pharma for Rigosertib in Latin America**
	February 12	**Closing of Underwritten Public Offering**
	January 17	**Moving Forward with INSPIRE Pivotal Trial After Promising Interim Analysis**
	January 4	**CRADA for Rigosertib in RASopathies with the National Cancer Institute**
2017	December 19	**License/Collaboration with HanX for ON 123300 (CDK4/6 + ARK5) inhibitor**

FINANCIAL DETAILS & SUMMARY

Onconova founded in 1998; public since 2013

Ticker	Nasdaq ONTX	**Debt**	$0
Stock Information	▪ ~79 million common shares outstanding ▪ Public float ~95% ▪ YTD average daily volume: 619,000	**Liquidity**	▪ Cash and cash equivalents of $7.3 million as of 03-31-2018 ▪ Excludes ~$29 million raised in financing in 2Q2018
Ownership*	683 Capital, EcoR1 Capital, Armistice Capital, Tyndall, Sabby; insiders including Board and management	**Burn-rate**	~$5.5 million per quarter over the last 8 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 ▪ CDK 4/6 & ARK-5 compound ON 123300 partnered with HanX for Greater China ▪ Onconova retains rights to the rest of the world

**Ownership information not fully updated for most recent financing*

***Reports available upon request*

MANAGEMENT TEAM

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

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

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

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

Mark Guerin
Chief Financial Officer

- Barrier Therapeutics
- Cardiokine
- PriceWaterhouseCoopers

Manoj Maniar, Ph.D.	Senior VP, Product Development	Alcon, SRI
Wolfgang Meyer, Ph.D.	Sr. VP Regulatory Affairs GM, Onconova GmBh	Amgen, Micromet, GPC, Fujisawa
Michael Petrone, M.D.	VP Clin. Dev. Medical Affairs and Pharmacovigilance	GSK, Roberts, GPC

UPCOMING CATALYSTS AND PRESENTATIONS

- Presentations (will be updated periodically)
  - European Hematology Association (EHA): Stockholm, June 14-17
  - Rodman Healthcare Conference: New York, September 4-6
  - American Society of Hematology (ASH): San Diego, December 1-4
  - *Quarterly Earnings Calls*

- Development Milestones
  - Presentation of Expansion Phase 2 Combination Trial Data
    - Phase 3 trial protocol, potential Special Protocol Process
  - 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

- Business Development Activities
  - Additional regional alliances for Rigosertib
  - Additional alliances for CDK program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