BIO-Latin America Conference
Sao Paolo, Brazil

October 26-28 2016
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 cancer therapeutics
- IPO in 2013: NASDAQ ticker ONTX
- Phase 3 stage: focused on unmet medical needs
  - Lead compound rigosertib being developed world-wide
  - IV rigosertib in global Phase 3 trial for higher-risk MDS
  - Oral rigosertib completed enrollment of Phase 2 trial
- Funded to deliver multiple Phase 3 milestones in 2017

*MDS: A disease of the elderly, affecting bone marrow function; patients can progress to acute myeloid leukemia (AML)*
## Key Achievements: Last 10 months

<table>
<thead>
<tr>
<th>Month</th>
<th>Event</th>
</tr>
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<tbody>
<tr>
<td>December 2015</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; patient enrolled in U.S. for global Phase 3 INSPIRE trial of rigosertib for MDS</td>
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<tr>
<td></td>
<td>ASH Presentation of interim Phase 2 data for rigosertib oral + azacitidine combination</td>
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<td>March 2016</td>
<td>Publication of ONTIME (first Phase 3 trial of rigosertib in MDS) results in <em>Lancet Oncology</em></td>
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<td>1&lt;sup&gt;st&lt;/sup&gt; patient enrolled in Europe for INSPIRE trial</td>
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<td>April 2016</td>
<td>Publication of rigosertib mechanism of action in <em>Cell</em></td>
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<td>June 2016</td>
<td>ASCO presentation of INSPIRE trial design</td>
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<tr>
<td>July 2016</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; patient enrolled in Japan for INSPIRE trial</td>
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<td>Oversubscribed rights offering closed; gross proceeds of $17.4 million</td>
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<tr>
<td>September 2016</td>
<td>Successful End-of-Phase 2 meeting for oral rigosertib + azacitidine; pivotal trial ahead</td>
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# Onconova Product Pipeline

<table>
<thead>
<tr>
<th>Program</th>
<th>Partnership</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>NDA/MAA</th>
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<tbody>
<tr>
<td>Single-agent IV rigosertib</td>
<td></td>
<td>2^{nd}-line Higher-risk (HR-MDS)</td>
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<td></td>
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<td><strong>Drug Name</strong></td>
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<tr>
<td>Oral rigosertib + azacitidine</td>
<td><strong>Partnership</strong></td>
<td>1^{st}-line Higher-risk (HR-MDS)</td>
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<td></td>
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<td><strong>Key Focus</strong></td>
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<td><strong>INSPIRE Pivotal Trial; interim analysis expected in 2017</strong></td>
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<td></td>
<td></td>
<td><strong>End-of-Phase 2 Meeting with FDA conducted</strong></td>
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<tr>
<td>IV Briciclib</td>
<td>Solid tumors</td>
<td>Dose-escalation Phase 1 Trial**</td>
<td></td>
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<td><strong>eIF4E targeting</strong></td>
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<tr>
<td>Recilisib</td>
<td>Global &amp; regional partnership opportunities</td>
<td>Non-Human Primate Efficacy</td>
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<td><strong>Targets radiation-induced apoptosis</strong></td>
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<td></td>
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<td><strong>Supported by U.S. Government funds</strong></td>
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<tr>
<td>ON 123300</td>
<td>CDK4/6 overactive tumors</td>
<td>Pre-IND Stage</td>
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<td></td>
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<td></td>
<td><strong>ARK5+CDK4/6 Targeting</strong></td>
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*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 targeting RAS pathways

- Phase 3 INSPIRE trial enrolling higher-risk MDS patients
  - Pre-planned interim analysis in H2-2017
  - Top-line data expected in 2018

- Phase 2 oral rigosertib + azacitidine trial completed enrollment
  - Successful End-of-Phase 2 meeting with FDA conducted in September 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

Published in *Cell*, 2016
Two Rigosertib Formulations

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

- Oral (Phase 2 enrolled)
  - Bioavailability ~35%
  - >250 patients treated
  - Combination with azacitidine advancing to pivotal trial
MDS Overlaps with Other Diseases

- MDS, malignant hematopoietic stem cell disorders characterized by:[1]
  - Bone marrow failure
  - Resultant cytopenias
  - Dysplastic morphology
  - Genetic abnormalities
  - Tendency to progress to AML

- MDS clinical and histopathological characteristics can overlap with many other hematological disorders
- BM biopsy is required to detect dysplasia, determine blast %, and obtain samples for cytogenetic/molecular studies
- Patient have a spectrum of risk, from low to very high, measured by IPSS-R scores.
- Current US prevalence estimate is ~59,000, with ~18,000 with higher risk MDS
- Treatment options limited to hypomethylating agents, approved more than a decade ago
- No second-line treatment approved

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Slide credit: clinicaloptions.com

Statistical analysis: two analyses planned

- Power 0.80; Target HR < 0.625; (reduce mortality by > 37.5%)
- $\alpha$ for ITT = 0.04; $\alpha$ 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

Patient Population for Phase 3 INSPIRE Trial

Data from ONTIME paper* published in *Lancet Oncology*

### ITT for ONTIME Trial

- **299 Patients**
- **ITT OS analysis of ONTIME** – HR = 0.87; NS survival benefit

### Subpopulation for INSPIRE Trial (ONTIME subset)

- **116 Patients**
- **ITT OS of proposed INSPIRE population** – HR = 0.48; P = 0.0008

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Global INSPIRE Trial Progress
225 Patients; 171 Prospective Sites in 21 Countries on 4 Continents

The INternational Study of Phase III IV Rigosertib, or INSPIRE, is based on guidance received from the U.S. Food and Drug Administration and European Medicines Agency and derives from findings of the ONTIME Phase 3 trial. Our partner SymBio is enrolling in Japan after discussions with the PMDA.

As of August 2016

*Patients enrolled in these countries
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
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)

Phase 2 Rigosertib + Azacitididine

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

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

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

Combination Program to Enter Pivotal Stage

- Successful End-of-Phase 2 meeting with FDA in September 2016

- Agreement reached on patient population and primary approval endpoint
  - First-line higher-risk MDS patients
  - Composite response endpoint comprising CR + PR

| Key Parameters and Milestones for Oral Rigosertib + Azacitidine Program |
|---|---|
| **Phase 3 Design** | Randomized Controlled | 1:1 randomization between Aza + placebo and Aza + oral rigosertib |
| **Primary Endpoint** | Composite Response | Complete and Partial Remission per IWG 2006 criteria for MDS |
| **Regulatory Path** | To be explored | Special Protocol Assessment (SPA), Fast-track and BTD* |
| **Phase 2 Data** | ASH 2016 | Safety and efficacy, duration of response, subgroups |
| **Final protocol** | After FDA/EMA review | H1-2017 |

*Breakthrough Designation
Pivotal Trial Timelines

Timeline for INSPIRE Global Trial

- First Patient Q4 2015
- Interim Analysis H2 2017
- Full Enrollment H2 2017
- Top-line Data H1 2018

Timeline for Pivotal trial of Oral Rigosertib + Azacitididine

- EOP2* Meeting Q3 2016
- Phase 2 Data ASH 2016
- Trial Protocol H1 2017
- Phase 3 Start H2 2017

*EOP2: End of Phase 2 meeting: completed in September 2016
Pipeline Beyond Rigosertib

- 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 Phase 1
  - ON 123300 (ARK5+CDK4/6 inhibitor) in advanced preclinical stage

*Onconova is seeking regional and worldwide partnerships
**Trial on hold pending manufacturing of new product lot;***Acute Radiation Syndrome
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 to enter Pivotal trial in 2017
  - 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
Presentations and Conferences

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
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<tbody>
<tr>
<td>October 17</td>
<td>ONTX sponsored KOL Analyst/Investor event on RAS as a therapeutic target, NYC</td>
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<tr>
<td>October 18-19</td>
<td>BIO Investor forum, San Francisco</td>
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<tr>
<td>October 26-28</td>
<td>BIO Latin America, Sao Paolo, Brazil*</td>
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<td>November 7-9</td>
<td>BIO Europe, Cologne, Germany*</td>
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<tr>
<td>December 3-6</td>
<td><strong>ASH conference, San Diego (Combination Phase 2 trial data presentation)</strong></td>
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