Developing Targeted Therapeutics

Providing Safe and Effective Treatment Options for Patients with Leukemias, Lymphomas and Solid Tumor Cancers
Forward-Looking Statements

Certain statements in this presentation are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of words such as "anticipate," "believe," "forecast," "estimated" and "intend" or other similar terms or expressions that concern Trovagene's expectations, strategy, plans or intentions.

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Investment Thesis
Nasdaq: TROV

Oncology Drug Development Expertise

► Onvansertib – only first-in-class, 3rd generation oral Polo-like Kinase 1 (PLK1) inhibitor in development

► Three active Investigational New Drug (IND) Applications: Hematologic and Solid Tumor Cancers

► Completed and published Phase 1 study in solid tumor cancers

► Orphan Drug Designation in Acute Myeloid Leukemia (AML) in the U.S. and Europe

► Biomarker strategy to identify patients most likely to respond to treatment

► Funding to advance development programs well into 2019

Attractive Investment Thesis

► Clinical development programs in three key indications of significant medical need for new treatment options
  – Phase 1b/2 in Acute Myeloid Leukemia in combination with standard-of-care chemotherapy
  – Phase 2 in metastatic Castration-Resistant Prostate Cancer in combination with Zytiga®
  – Phase 1b/2 in metastatic Colorectal Cancer in combination with FOLFIRI + Avastin®

► Working with leading investigators and cancer institutions across the U.S.

► Demonstrated synergy of onvansertib in combination with standard-of-care drugs

► Proven safety, tolerability and preliminary data demonstrating treatment response

► Patent protection out to 2032 and beyond
Onvansertib Market Opportunity

Market Potential By Indication Per Year of Treatment
Estimated Total ~10.5 Billion\(^1\)

Sales ($ Millions)

- AML: 650
- Colorectal: 1,265
- Prostate: 1,470
- Pancreatic: 2,216
- Breast: 2,070
- Small Cell Lung: 1,750
- Ovarian: 1,056

Approximate Year of FDA Approval

2020 2021 2022 2023 2024 2025 2026 2027 2028

Licensed Global Development & Commercialization Rights to Onvansertib (PLK1 Inhibitor) from NMS

- Largest oncology research and development company in Italy and highly regarded throughout Europe and US
- Leader in protein kinase drug development (Polo-like Kinase Inhibitors)
- Identification and validation of molecular targets focused on driver oncogenes
- Excellent track record licensing innovative drugs to pharma/biotech companies including: Genentech (Roche), Ignyta (Roche), Novartis
- Oncology specialized contract development and manufacturing organization
- cGMP compliant and FDA validated production of API (active pharmaceutical ingredient) and finished dosage forms
- Analytical services, clinical supply management and CMC regulatory support
Excellent track record licensing innovative drugs to pharma/biotech companies that have subsequently received FDA breakthrough status and priority review designation.

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<th>Phase 2</th>
<th>Phase 3</th>
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Partnering Strategy

► Engaging in clinical trial collaborations across a number of major tumor types

► Identifying regional pharma partners for collaboration (Japan, Europe)

► Establishing partnerships to fund clinical trials (Phase 1b/2 mCRC)
Strategy for Developing Onvansertib

- 3 active INDs in place enabling clinical development in hematologic and solid tumor cancers
- Leveraging a proven cancer target, PLK1
- Integrating biomarkers to identify patients most likely to respond to treatment
- Orphan Drug Designation in AML
- Combination therapy with already approved drugs
  - Phase 1b/2 trial of onvansertib + cytarabine or decitabine in Acute Myeloid Leukemia (AML)
  - Phase 2 trial of onvansertib + Zytiga® in metastatic Castration-Resistant Prostate Cancer (mCRPC)
  - Phase 1b/2 trial of Onvansertib + FOLFIRI and Avastin® in metastatic Colorectal Cancer (mCRC)
- Phase 1b/2 trial-ready in pancreatic, ovarian, breast and lung cancer
### Onvansertib – Pipeline Within a Molecule Opportunities in Leukemias/Lymphomas and Solid Tumors

- **Three active Investigational New Drug (INDs) Applications in place with the FDA**

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<th>Phase 1</th>
<th>Phase 2</th>
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<td>Metastatic Castration-Resistant Prostate (CRPC)</td>
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<td><em>Phase 2 trial in combination with Zytiga® (abiraterone acetate)/prednisone</em></td>
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<td></td>
<td>Small Cell Lung</td>
<td><em>Phase 1b/2 trial ready</em></td>
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**Solid Tumor Cancers**

- Pancreatic
- Ovarian
- Breast
- Small Cell Lung

*Zytiga® is a registered trademark of Janssen Biotech, Inc.*
Advancement of PLK Inhibitor Drug Class

1st Generation PLK Inhibitors
- GSK – 461364
- BI – 2536

2010 - 2014
- Limited Clinical Activity
- Off-Target Toxicities
- PanPLK Inhibitors
- IV (Intravenous Formulation)

2nd Generation PLK Inhibitors
- BI – Volasertib

2012 - 2016
- PLK1 Proven Drug Target
- PanPLK IV Long Half-life
- Phase 2/3 Trials in Combination with SOC demonstrated Clinical Response
- Lethal Infections Led to Discontinuation
Onvansertib: First-in-Class, 3rd Generation PLK1 with Best-in-Class Attributes
Onvansertib: Selective Only for PLK1
No Off-Target Adverse Events

► PLK1 is a master regulator of cell division

► Onvansertib has demonstrated safety and tolerability

► Phase 1 Safety Study:
  – No dose-limiting toxicities at the recommended Phase 2 dose (24 mg/m²)
  – No gastrointestinal, mucositis or alopecia
  – Expected myelosuppressive effects observed (thrombocytopenia and neutropenia) deemed related to the mechanism-of-action and reversible
  – No other clinically relevant safety findings were observed
PLK1: Established Target for Cancer Therapy

PLK1 Plays a Critical Role in Initiation, Maintenance and Completion of Mitosis

► Polo-like Kinase 1 (PLK1)
  - Belongs to a family of kinases (PLK1,2,3,4,5)
  - Dysfunction leads to cancer formation and progression
  - Over-expressed in dividing cancer cells
  - Inhibition leads to cancer cell death

1Liu et al- PLK1, A Potential Target for Cancer Therapy; Translational Oncology – Vol. 10 – pp. 22-32; February 2017
Onvansertib: Highly-Selective Only for PLK1

Selective PLK1 Inhibitor
► Tested against >260 kinases
► PLK1 was the only active target (IC$_{50}$ of 2nM)

Causes cancer cell death by G$_2$M arrest
► Onvansertib blocks cell division (mitosis)

<table>
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<th>PLK Member</th>
<th>Onvansertib IC$_{50}$* (μM)</th>
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<tr>
<td>PLK1</td>
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<tr>
<td>PLK2</td>
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<tr>
<td>PLK3</td>
<td>&gt; 10</td>
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1Data on File, Trovagene, Inc.
Onvansertib Combination Therapy Strategy

- Cornerstone of precision cancer medicine
- Demonstrated synergy with chemotherapies and targeted therapeutics
- Enhances efficacy (targets key pathways by synergy or additive effect)\(^1\)
- Reduces drug resistance, while providing therapeutic benefits

\(^1\)Mokhtari, R et al - Combination Therapy in Combatting Cancer – Oncotarget, 2017, Vol. 8 (No. 23), pp: 38022-38043
Onvansertib: Synergy May Enhance Efficacy of Standard of Care (SOC) Therapies

Onvansertib Synergistic in Combination with SOC Therapies

1Data on File, Trovagene, Inc.

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Clinical Trial Roadmap

Acute Myeloid Leukemia (AML)

Metastatic Castration-Resistant Prostate Cancer (mCRPC)

Metastatic Colorectal Cancer (mCRC)

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Acute Myeloid Leukemia\(^1\)
Significant Need for New Treatment Options

- Aggressive hematologic malignancy of immature blood cells
- 20,000 new cases, 10,400 deaths annually, and 5 year survival rate of 25%
- Treatment options vary based on patient condition / age, but can include:
  - Chemotherapy / Radiation / Stem Cell Transplant
- Preclinical *in-vitro* and *in-vivo* data demonstrate efficacy of Onvansertib* as single agent and in combination with drugs used to treat AML

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\(^1\)National Cancer Institute SEER 2016; \(^2\)Valsasina et al., Mol Cancer Ther; 11(4) April 2012

*Orphan Drug Designation granted for Onvansertib by the FDA September, 2017 and by the EMA in July, 2018; *National Cancer Institute SEER 2016; *Valsasina et al., Mol Cancer Ther; 11(4) April 2012
Onvansertib Positioning in AML Patient Selection Algorithm

AML Diagnosis

18,376\(^1\) cases/year

Eligible for Induction Treatment

~11,000

Ineligible for Induction Treatment

~7,400

Responders

50-70%

Consolidation Treatment

Eligible for Induction Treatment

~11,000

Relapsed & Refractory

30-50%

3,300 to 5,500

Onvansertib in combination with standard-of-care chemotherapy and/or targeted therapeutics\(^2\)

\(^1\)Visser et al. (2012), Eur J Cancer (48). Estimated cases in EU27 per year; \(^2\)e.g. Midostaurin for FLT3 mutation
Ongoing Phase 1b/2 Clinical Trial in AML

**Onvansertib in Combination with Either Low-Dose Cytarabine or Decitabine in Patients with Acute Myeloid Leukemia (AML)**

**Phase 1b:** Dose escalation to assess safety and identify recommended Phase 2 dose

- Administered orally, once daily on days 1-5 of each cycle (21-28 days)

**Phase 2:** Assess safety and preliminary antitumor activity

- **Efficacy Endpoints:** Rate of complete response (CR + CRi) defined as morphologic leukemia-free state (MLF)
- **Exploratory Endpoints:** Evaluation of pharmacodynamic and correlative biomarkers
Anti-Leukemic Activity

- Of the 26 patients evaluable for safety, 19 patients had an evaluable bone marrow biopsy to assess anti-leukemic activity.
- Preliminary efficacy in the evaluable population showed includes 3 patients achieving complete response (CR) and 1 patient achieving complete response with incomplete hematologic recovery (CRi).

**Onvansertib + Decitabine**

- CR occurred at onvansertib 27mg/m²

**Onvansertib + LDAC**

- Ongoing
- PR
- SD
- CRi
- CR
- MLFS
- PD
- * No BM data

Data Labels represent onvansertib dose (mg/m²)

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Patient Cases

► 07-035: 76 year-old male, diagnosed with AML in 2015; treated with induction chemotherapy; relapsed in December 2018; entered trial in January 2019 on onvansertib 40mg/m² + decitabine
► Patient reached CR as of the end of cycle 2 and is currently in cycle 3
► % bone marrow blasts decreased from 20% (at screening) to less than 5% at the end of cycle 2; circulating blasts remained low during the entire treatment (0.2% to 2.2%)

► 03-037: 83 year-old male with prior Cytarabine and Decitabine treatment. 7+3 Decitabine maintenance; entered trial in December 2018 on onvansertib 40mg/m² + Cytarabine
► Patient reached MLFS at then end of cycle 2 and CR at the end of cycle 4
► % bone marrow blasts decreased from 10% (at screening) to 4% (cycle 2)

► 07-009: 75 year-old male, diagnosed with AML in 2009; treated with induction chemotherapy; relapsed March 2018; entered trial April 2018 on onvansertib 12mg/m² + decitabine
► Onvansertib dose increased to 18mg/m² cycle 6; 27mg/m² cycle 10
► Patient reached PR at end of cycle 4 and CR at the end of cycle 11
► % bone marrow blasts decreased from 94% (at screening) to <5% (cycle 11) and circulating blasts decreased from 92% (C1D1) to 2.2% (C11D22)

► 05-030: 68 year-old female with MDS progressed after 6 cycles of azacytidine; diagnosed with AML in September 2018; entered trial in October 2018 on onvansertib 27mg/m² + decitabine
► Onvansertib dose reduced to 18mg/m² at cycle 5
► Patient reached CRi at then end of cycle 4 and is in cycle 6
► % bone marrow blasts decreased from 20% (at screening) to 1% (cycle 4) and circulating blasts decreased from 43% (C1D1) to 1% (C4D21)
PLK1 Inhibition Can Be Monitored Through pTCTP Status

► pTCTP as a marker of PLK1 activity:
  - PLK1 phosphorylates the translational control tumor protein (TCTP) on serine 46\(^1\)
  - pTCTP was identified as a specific marker for PLK1 activity in in-vivo preclinical models\(^1\)

► In the Phase 1b AML trial, 8 out of the 22 subjects (36\%) tested showed a decrease in % pTCTP at 3h post-dose compared to pre-dose

\(^1\)Cucchi et al., Anticancer Res., 2010
PLK1 Inhibition by Onvansertib is Correlated with Higher Response to Treatment

- Patients with target engagement had a significantly higher decrease in bone marrow blasts compared to patients with no-target engagement.
- 4 out of the 7 patients with target engagement had a decrease in bone marrow blasts ≥50%.
- Conversely, only 1 out of the 9 patients with no-target engagement showed a decrease in bone marrow blasts upon treatment.

% Bone Marrow Blast Change Relative to Baseline

% Bone Marrow Blast Reduction from Baseline

*patient sample had low % circulation blasts (~1%) and showed a 40% reduction in pTCTP.*
Simple Blood Test for Predicting Response to Onvansertib

- Biomarker assay uses a blood sample to test whether a patient has a greater likelihood to respond to Onvansertib
- If patient is positive for biomarker assay, then drug is administered
- Blood test examines the extent that Onvansertib inhibits PLK1 enzymatic activity (called target engagement) within circulating cancer cells

**In-vivo sampling (current method)**

- Pre-dose sample
- Patient receives a single dose of onvansertib
- 3h post-dose sample
- Assess target engagement

**Ex-vivo sampling (in development)**

- Obtain 2 vials of blood from patient
- Control vial, Vehicle
- Treat blood sample with onvansertib or vehicle control
- Treatment vial, Onvansertib
- Assess target engagement

<table>
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<tr>
<th>Onvansertib</th>
<th>pTCTP</th>
<th>TCTP</th>
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(Treatment vial, Vehicle; Control vial, Onvansertib)
Metastatic Castration-Resistant Prostate Cancer
Opportunity to Increase Duration of Response to Therapy

► 25,000 men die from metastatic prostate cancer annually and the five-year survival rate is 37%²

► Treatments
  – Zytiga® (Johnson & Johnson)/prednisone
  – Xtandi® (Astellas/Pfizer)

► Ongoing need to increase duration of response to treatment
  – Patients develop resistance within 9-15 months⁴ and do not respond well to subsequent therapies

► Preclinical studies demonstrate synergy between Onvansertib and Zytiga®
  – PLK1 inhibition improves abiraterone efficacy by repressing the androgen signaling pathway³,⁴

Ongoing Phase 2 Clinical Trial in mCRPC

Onvansertib in Combination with Zytiga® and Prednisone in Patients with Metastatic Castration-Resistant Prostate Cancer (mCRPC)

**Dosing Regimen**

**Arm A**
- Onvansertib – 24 mg/m²
  - Days 1-5 (21-Day Cycle) + Abiraterone daily
- Duration: 4 Cycles = 12 Weeks
- Evaluation: Disease Control
  - PSA Stabilization or Decline

**Arm B**
- Onvansertib – 24 mg/m²
  - Days 1-5 (14-Day Cycle) + Abiraterone daily
- Duration: 6 Cycles = 12 Weeks
- Evaluation: Disease Control
  - PSA Stabilization or Decline

**Efficacy Endpoints**
Effect of Onvansertib in combination with Zytiga®/prednisone on disease control assessed by prostate-specific antigen (PSA) decline or stabilization pre- and post-treatment

**Safety Endpoint**
Safety of Onvansertib in combination with Zytiga®/prednisone

**Exploratory Endpoint**
Target inhibition of PLK1, evaluation of relevant biomarkers and correlation with patient response and genomic profile
Early PSA Response Observed with Addition of Onvansertib to Daily Zytiga®

- 6 patients have completed 4 cycles (3 months) of treatment with onvansertib + abiraterone
- 2 of 6 patients had observed declines in PSA levels after dosing with onvansertib
- To date, 1 patient has achieved the efficacy endpoint of disease stabilization based on PSA levels (primary endpoint)

PSA trajectory in patient achieving primary efficacy endpoint changed from 100% increase (16.05ng/ml to 34.23 ng/ml) in the 60 days prior to adding Onvansertib to only an 8.4% increase during 84 days on treatment

Tumor assessed at Cycle1 Day 1 as a variant known as AR-V7, considered an aggressive tumor that is resistant to anti-androgen therapy
Colorectal Cancer: Unmet need in mCRC

- 140K new cases of CRC in 2018 with 64.5% 5 year survival\(^1\)
  - ~51K deaths per year from mCRC\(^1\)

- Tumor biomarkers drive therapy decisions for 1\(^{st}\) line mCRC therapy\(^2\)
  - ~50% mCRC is RAS mutant (Kras)
  - Targeted therapies exclude patients with RAS mutations

- Large unmet need in RAS mutant CRC\(^2\)
  - No targeted therapies are available for RAS mutant CRC
  - Standard-of-care is chemotherapy (FOLFOX/FOLFIRI)
  - 2\(^{nd}\) line therapies have ~5% response rate in metastatic CRC (mCRC)

Onvansertib: Synergy in Combination with Irinotecan (FOLFIRI)

- Combination of Onvansertib with Irinotecan significantly reduces tumor growth compared to either drug alone.

- In 3 independent models tested, Onvansertib induced maximal tumor regression of ~84% compared to vehicle.

- Kras mutation is a biomarker for Onvansertib sensitivity.

- KRAS mutated NIH3T3 cells showed higher sensitivity to Onvansertib compared to KRAS wild-type (WT) cells\(^1\)

\(^1\)Investigator Brochure, Data-on-file, Trovagene
Planned Phase 1b/2 Clinical Trial in mCRC

Onvansertib in Combination with FOLFIRI + Avastin for Second-Line Treatment of Metastatic Colorectal Cancer in Patients with a Kras Mutation

Phase 1b: Dose escalation to assess safety and identify recommended Phase 2 dose

- Administered orally, once daily on days 1-5 every 14-days (2 courses per 28-day cycle)

Phase 2: Assess safety and preliminary antitumor activity

- **Efficacy Primary Endpoint:** Objective response rate (ORR) in patients who receive at least 1 cycle (2 courses) of Onvansertib in combination with FOLFIRI and bevacizumab

- **Efficacy Secondary Endpoint:** Preliminary efficacy defined as complete response (CR) plus partial response (PR) plus stable disease (SD)
# Key Inflection Points – Q2’19 – Q1’20

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<td>✓ AACR Phase 1b Data Presentation (4/1)</td>
<td>✓ ESMO Phase 2 Data Presentation (9/27)</td>
<td>✓ ESH Phase 2 Data Presentation (10/24)</td>
<td>✓ MDS initial safety and efficacy data readout</td>
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<td>Myelodysplastic Syndrome (MDS) – Investigator Initiated</td>
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<td>✓ MDS – Investigator Initiated trial enrolling</td>
<td>✓ ASH Phase 2 Data Presentation (12/7)</td>
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<td>✓ AACR Data Presentation (4/2)</td>
<td>✓ Asian-Pacific Prostate Cancer Conference Presentation (8/24)</td>
<td>✓ EMUC Conference presentation of safety and preliminary efficacy from 14-day dosing schedule (11/14-17)</td>
<td>✓ ASCO-GU Phase 1b safety and efficacy data (2/13)</td>
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<td>metastatic Colorectal Cancer (mCRC)</td>
<td>✓ Sites activated and enrolling patients (5/1)</td>
<td>✓ Clinical collaboration with large-cap biotech</td>
<td>✓ Gastrointestinal Oncology Conference (10/10-11) Preliminary Phase 1b safety and efficacy data</td>
<td>✓ ASCO-GI Phase 2 efficacy data (1/23-25)</td>
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Thank You

For additional information please contact: ir@trovagene.com