Developing Targeted Therapeutics

Providing Safe and Effective New Treatment Options for Patients Most Likely to Respond

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Forward-Looking Statements

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Investment Thesis

Nasdaq: TROV

Oncology Drug Development Expertise

- Onvansertib – only first-in-class, 3rd generation 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 chemo
  - 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 who approached Trovagene
- Demonstrated synergy with Onvansertib in combination with already approved drugs
- Proven safety, tolerability and preliminary data demonstrating treatment benefit
- Patent protection out to 2032

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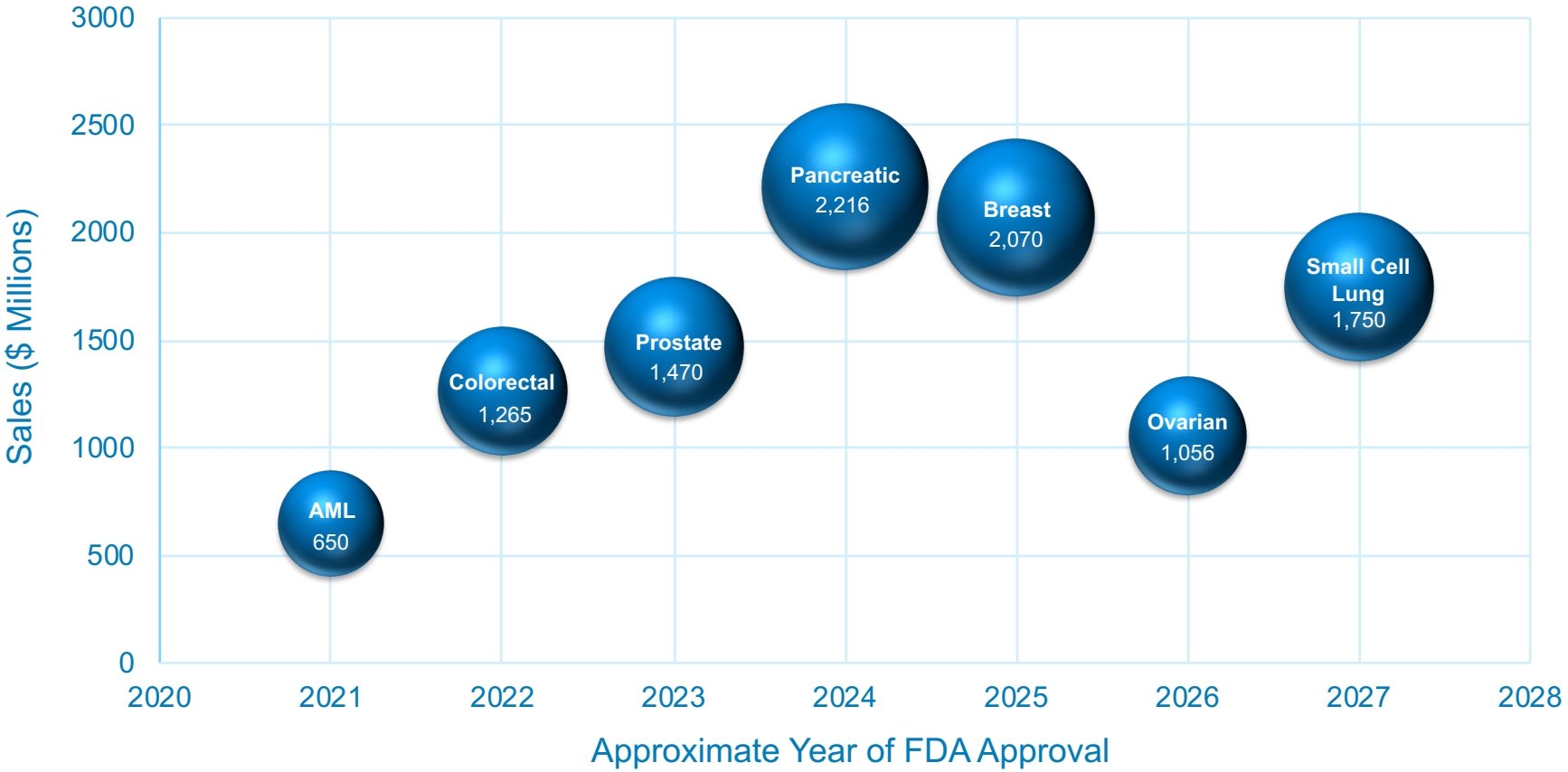
Onvansertib Market Opportunity

Market Potential By Indication Per Year of Treatment
Estimated Total ~10.5 Billion[1]



[1]2018 statistics https://seer.cancer.gov/statfacts/html/common.html

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

- Largest oncology research and development company in Italy
- Developed anthracycline class of drugs (doxorubicin)
- Leader in protein kinase drug development (Polo-like Kinase Inhibitors)

LOCATION:
Nerviano (15km from Milan) Italy

TOTAL SITE PROPERTY:
300.000 m²

NUMBER OF EMPLOYEES:
About 450

OPERATIONS:
Pharmaceutical Manufacturing

- 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

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Nerviano Oncology Portfolio Success

- Excellent track record licensing innovative drugs to pharma/biotech companies that have subsequently received FDA breakthrough status and priority review designation

Licensed	Preclinical	Phase 1	Phase 2	Phase 3	Registered
ARRAY BIOPHARMA	Encorafenib (B-RAF IP) Melanoma Braf mutation in combination with binimetinib				
Roche ignyta	Entrectinib (TRK, ROS, ALK) Non-Small Cell Lung				
tiziana LIFE SCIENCES	Milciclib (CDK, other kinases) Thymic Cancer				
trovagene ONCOLOGY	Onvansertib (PLK1 inhibitor) AML, mCRPC, mCRC				
SERVIER Oncology	MPS1 Inhibitor Solid Tumors				
Genentech A Member of the Roche Group	ADC (PNU-652)				
OXFORD BioTherapeutics	ADC (NMS-P945)				

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Strategy for Developing Onvansertib

- 3 active INDs in place
- Leveraging a proven cancer target, PLK1
- 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

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Onvansertib – Pipeline Within a Molecule
Opportunities in Leukemias/Lymphomas and Solid Tumors

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

	Preclinical	Phase 1	Phase 2
Leukemias & Lymphomas	Acute Myeloid Leukemia – Orphan Drug Designation in the U.S. and Europe *Phase 1b/2 trial in combination with low-dose cytarabine (LDAC) or Decitabine*		
	Metastatic Castration-Resistant Prostate (CRPC) *Phase 2 trial in combination with Zytiga® (abiraterone acetate)/prednisone*		
	Colorectal (CRC) *Phase 1b/2 trial in combination with FOLFIRI + Bevacizumab*		
Solid Tumor Cancers	Pancreatic *Phase 1b/2 trial ready*		
	Ovarian *Phase 1b/2 trial ready*		
	Breast *Phase 1b/2 trial ready*		
	Small Cell Lung *Phase 1b/2 trial ready*		

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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

PoC CAPITAL

integrium
Clinical Research

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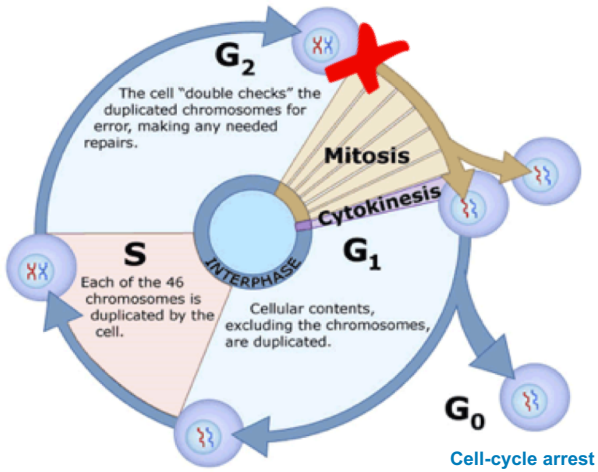
PLK1: Established Target for Cancer Therapy

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

[1]Liu et al- PLK1, A Potential Target for Cancer Therapy; Translational Oncology – Vol. 10 – pp. 22-32; February 2017

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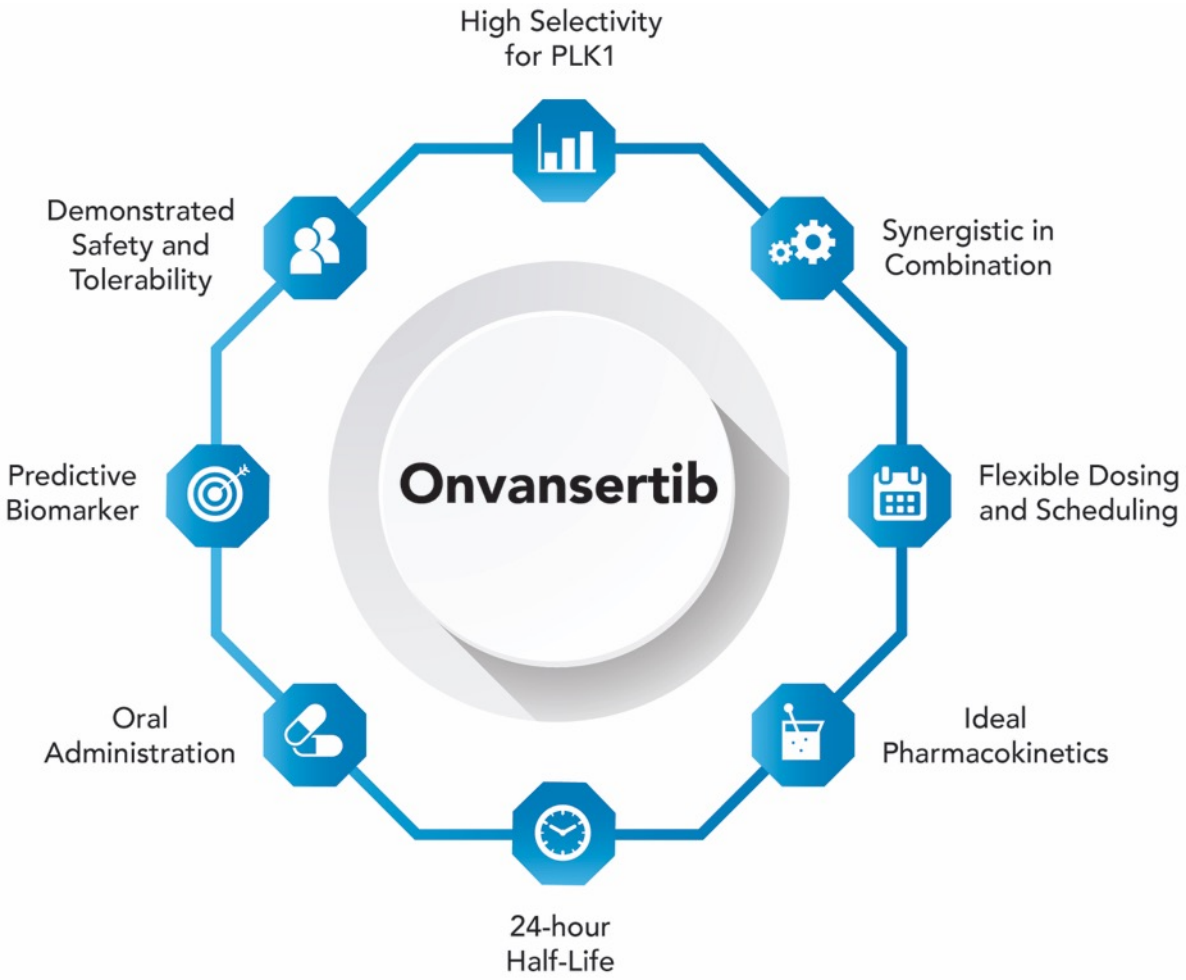
Onvansertib: First-in-Class, 3rd Generation PLK1 with Best-in-Class Attributes



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Onvansertib: Highly-Selective Only for PLK1

Selective PLK1 Inhibitor

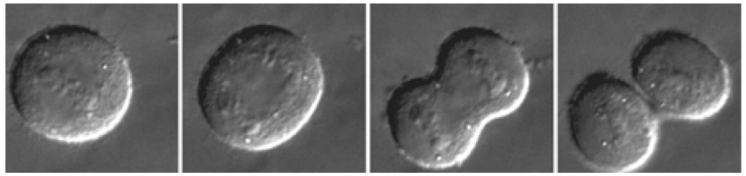
- Tested against >260 kinases
- PLK1 was the only active target (IC_{50} of 2nM)

PLK Member	Onvansertib IC50* (μM)
PLK1	0.002
PLK2	> 10
PLK3	> 10

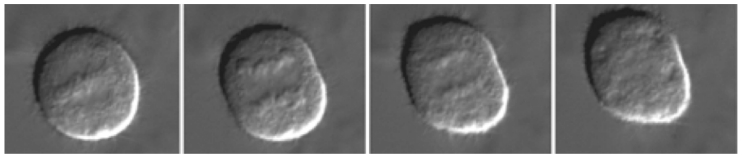
Causes cancer cell death by G_2M arrest

- Onvansertib blocks cell division (mitosis)

Tumor Cell Division



Onvansertib Blocks Tumor Cell Division



[1]Data on File, Trovagene, Inc.

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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

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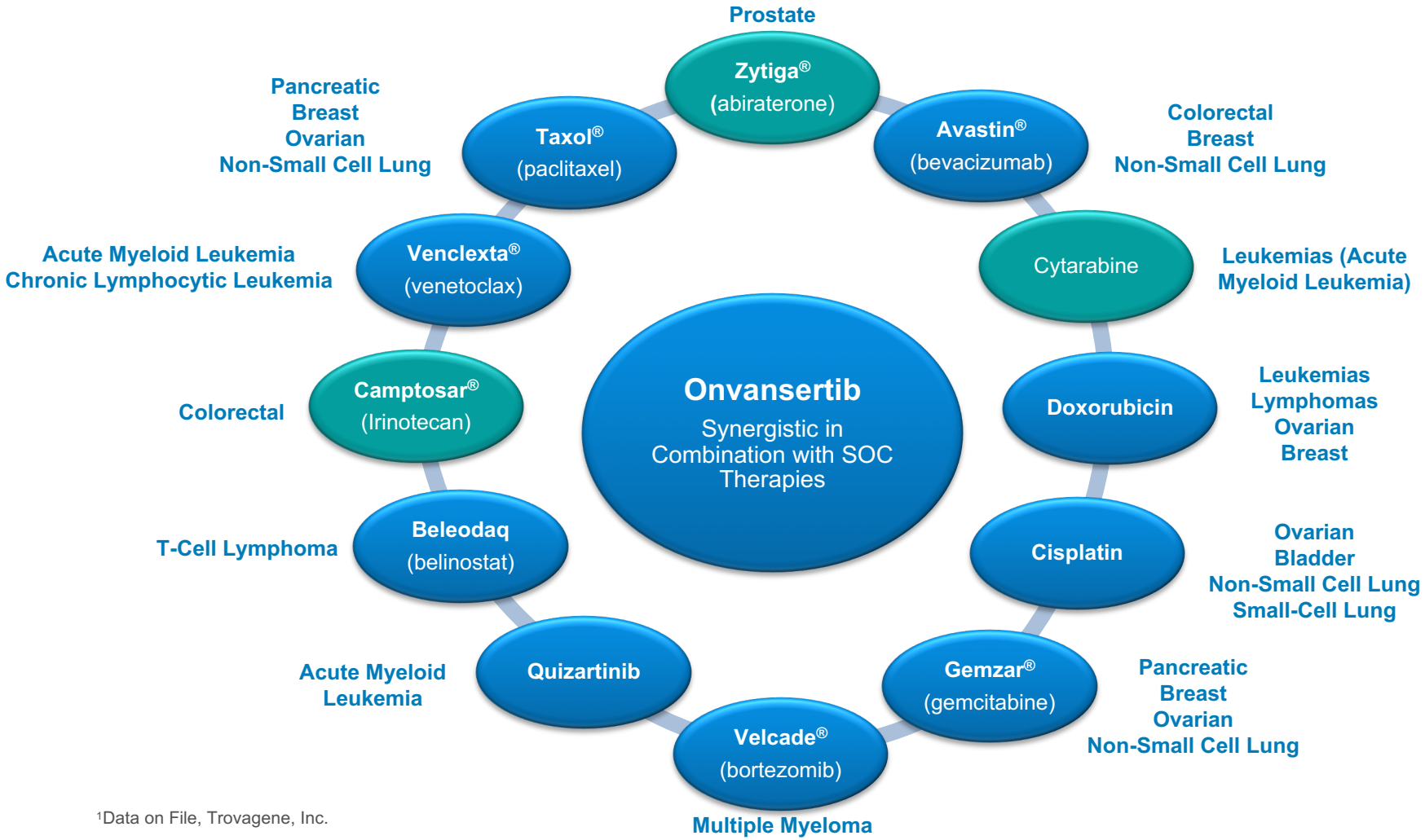
Onvansertib: Synergy May Enhance Efficacy of Standard of Care (SOC) Therapies[1]



[1]Data on File, Trovagene, Inc.

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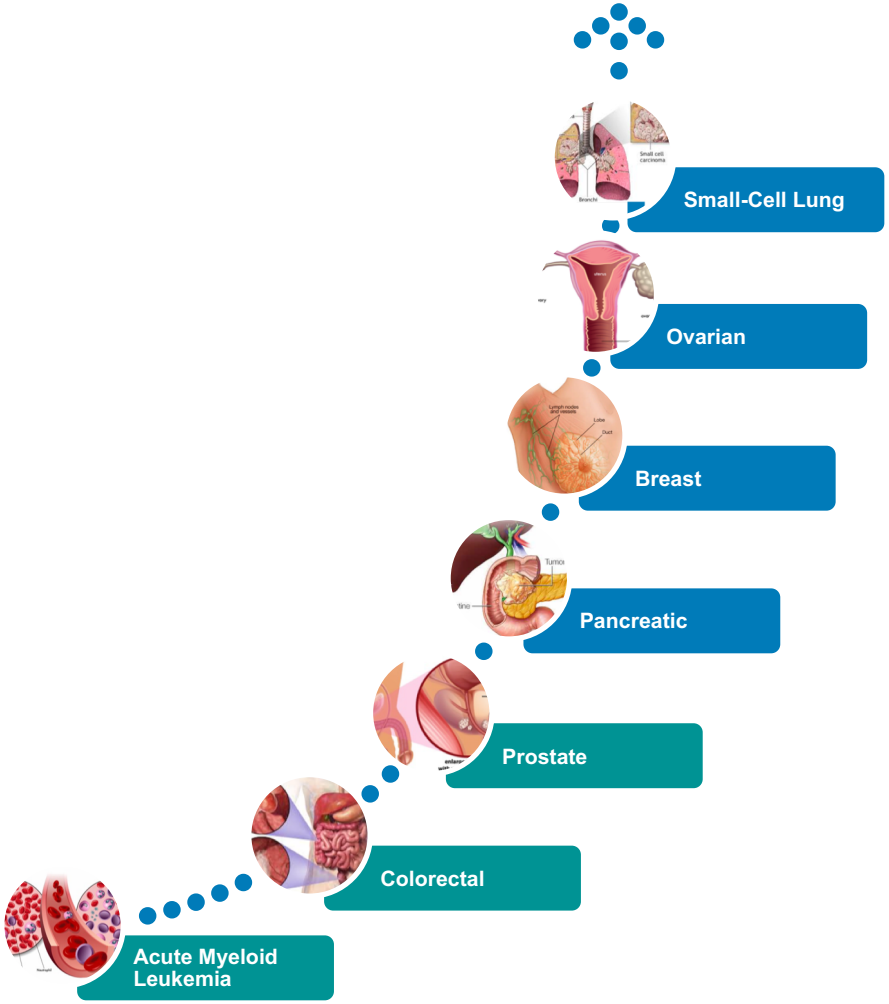
Onvansertib Clinical Development Roadmap



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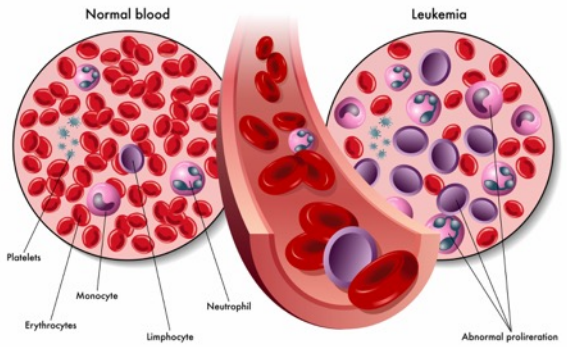
Acute Myeloid Leukemia[1]
Significant Need for New Treatment Options

- 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

Acute Myeloid Leukemia



*Orphan Drug Designation granted for Onvansertib by the FDA September, 2017 and by the EMA in July, 2018 ;[1]National Cancer Institute SEER 2016; [2]Valsasina et al., Mol Cancer Ther; 11(4) April 2012

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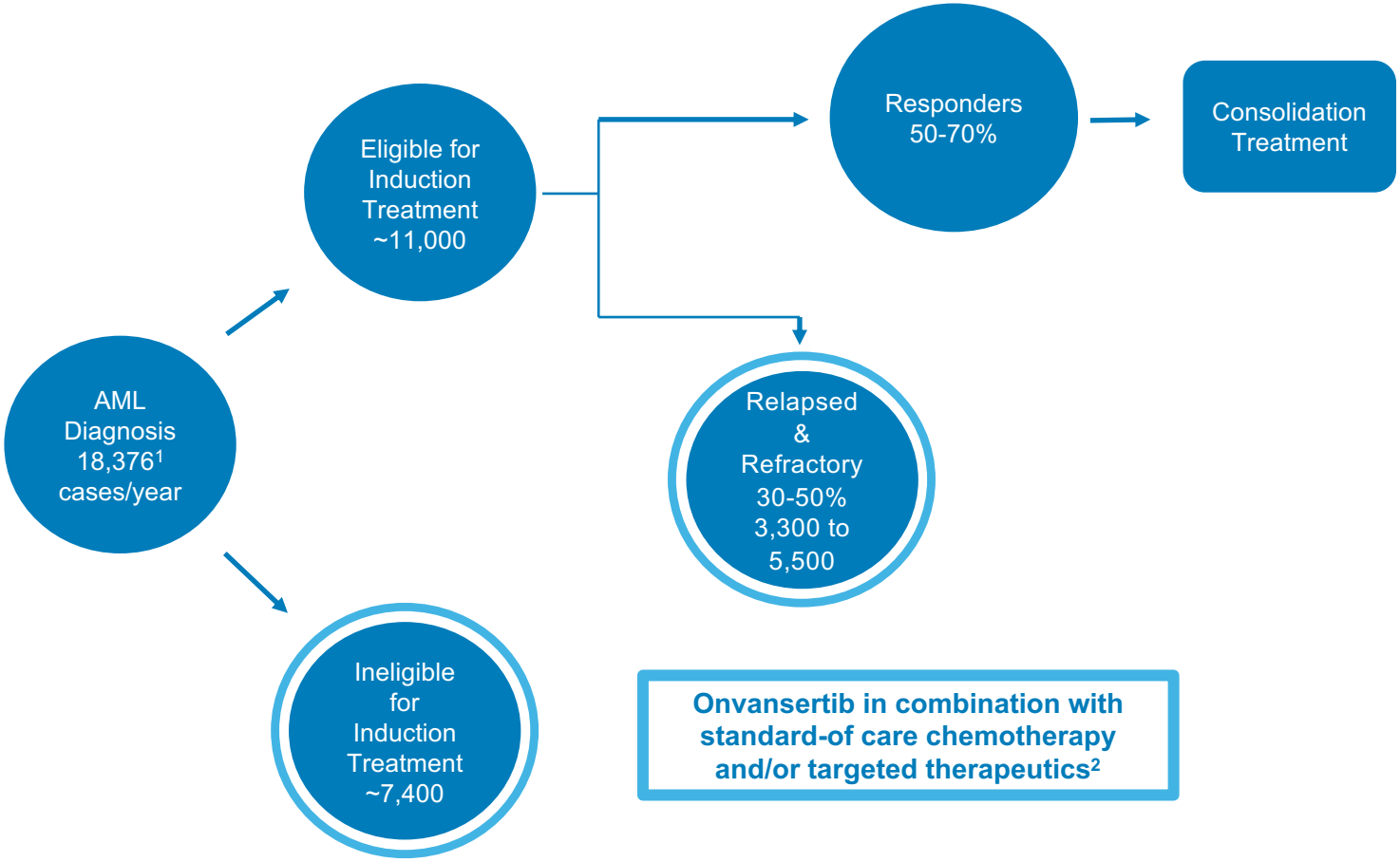
Onvansertib Positioning in AML
Patient Selection Algorithm



[1]Visser et al. (2012), Eur J Cancer (48). Estimated cases in EU27 per year; [2]e.g. Midostaurin for FLT3 mutation

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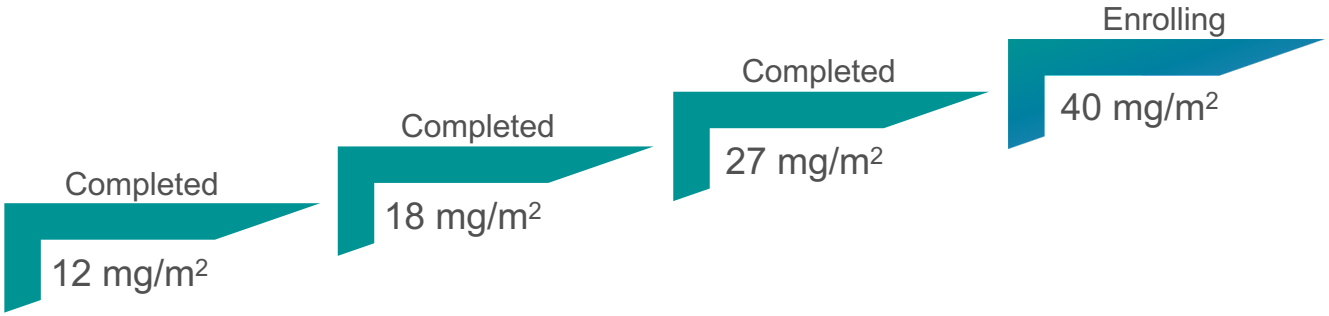
Ongoing Phase 1b/2 Clinical Trial in AML

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

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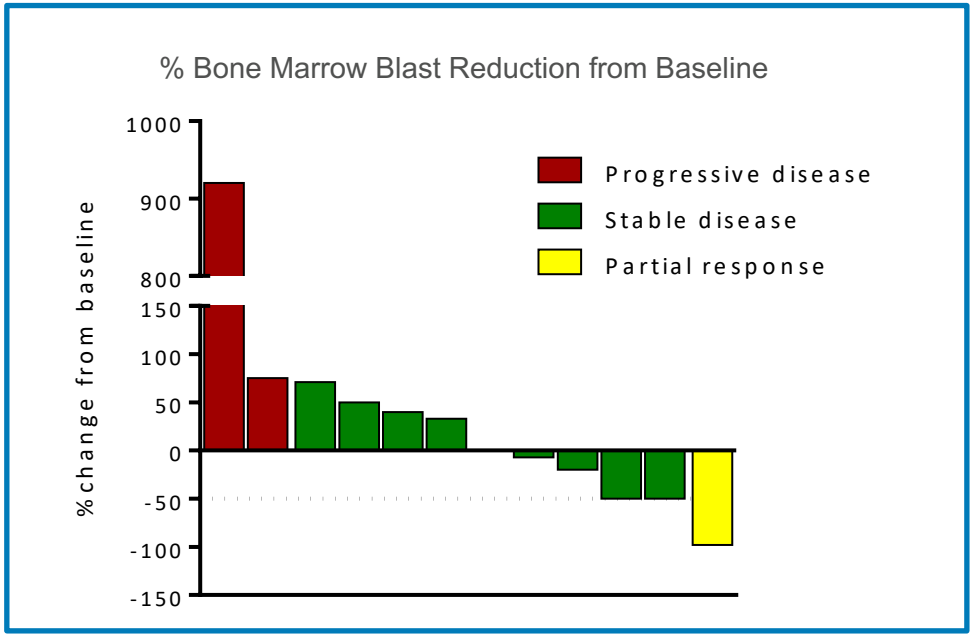
Phase 1b/2 Trial Anti-Leukemic Activity

- Phase 1b objective is to assess the safety and tolerability of Onvansertib in combination with standard-of-care chemotherapy
- Of the 19 patients evaluable for safety, 12 patients had an evaluable bone marrow biopsy to assess anti-leukemic activity based on criteria from the 2017 ELN recommendations[1]
- Of the 12 patients evaluated for preliminary anti-leukemic activity, 1 patient had a PR, 9 patients had SD and 2 patients had PD[2]



[1] Dohner et al., Blood, 2017. [2] American Society of Hematology (ASH) Conference Poster Presentation - December 2018

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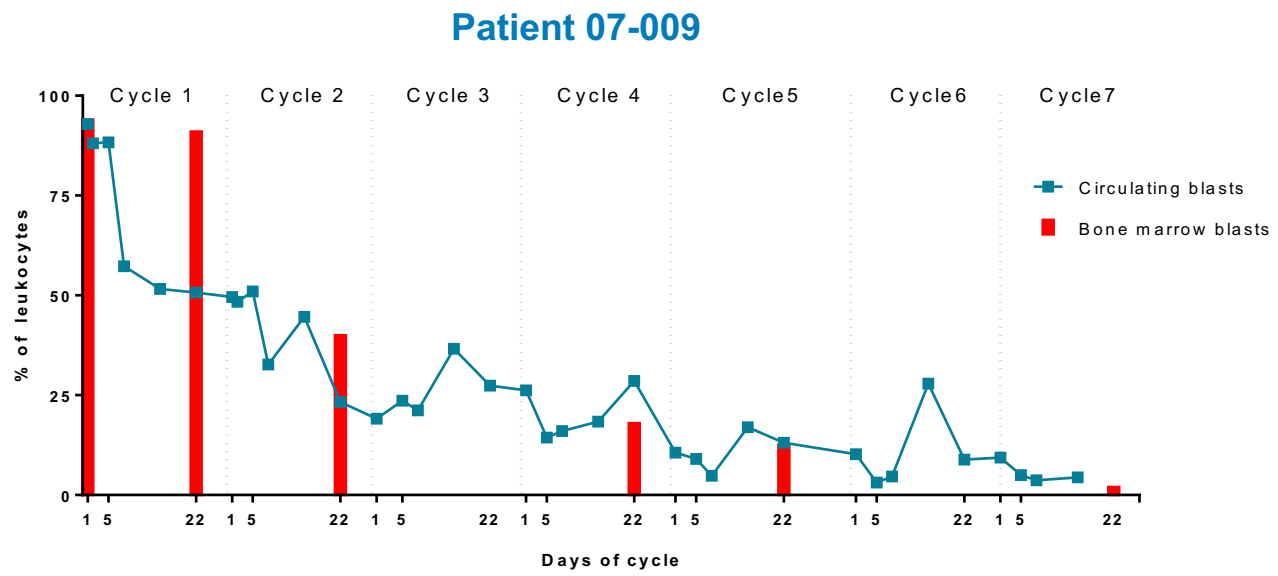
Patient Case Overview[1]

- 75 year-old male, diagnosed with AML in 2009 and treated with induction chemotherapy; relapsed in March 2018 and entered trial in April 2018 on Onvansertib + Decitabine
- Onvansertib entry dose of 12 mg/m^2 and was increased to 18 mg/m^2 at cycle 6
- Patient reached PR as of the end of cycle 4 / beginning of cycle 5 and is currently on cycle 8 of treatment
- % bone marrow blast decreased from 94% (at screening) to 2% (cycle 7) and circulating blasts decreased from 92% (C1D1) to 4% (C7D15)



[3] American Society of Hematology (ASH) Conference Poster Presentation - December 2018

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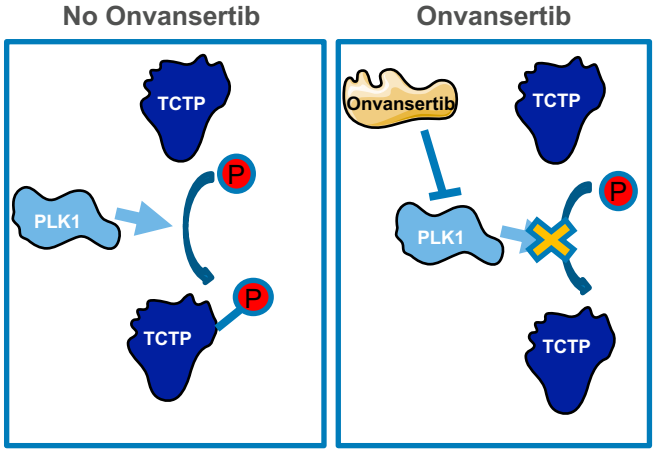
PLK1 Inhibition Can Be Monitored Through pTCTP Status

- 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]



[1]Cucchi et al., Anticancer Res., 2010

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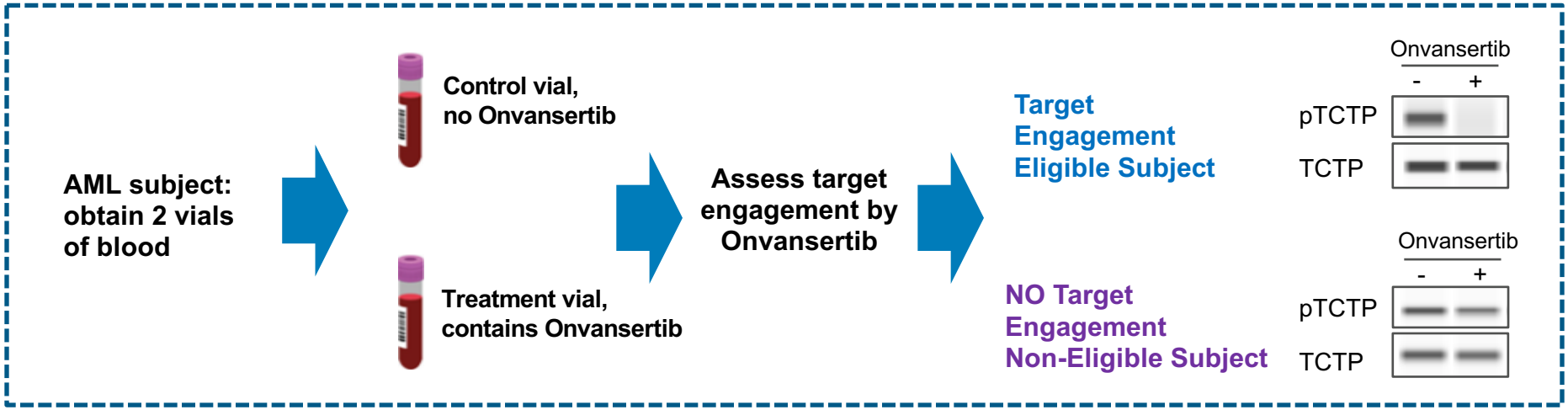
Simple Blood Test for Predicting Response to Onvansertib

- 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



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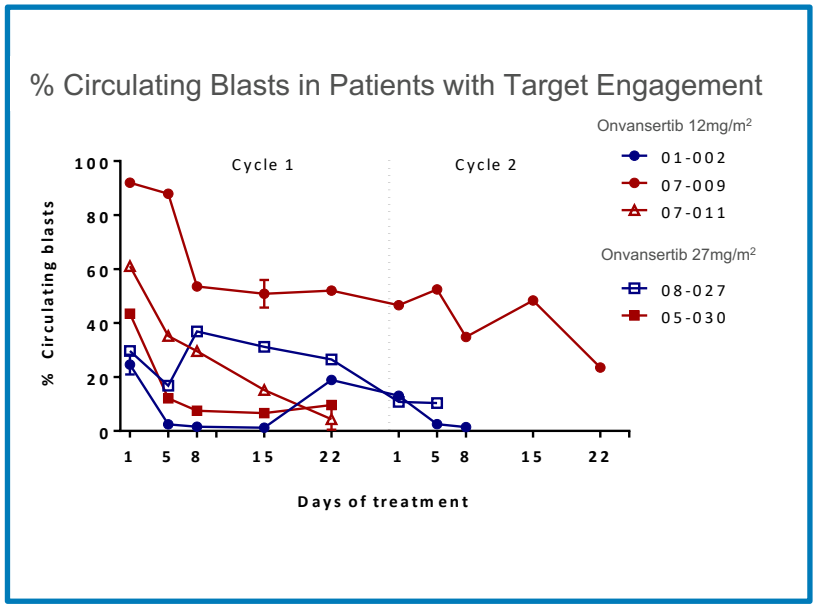
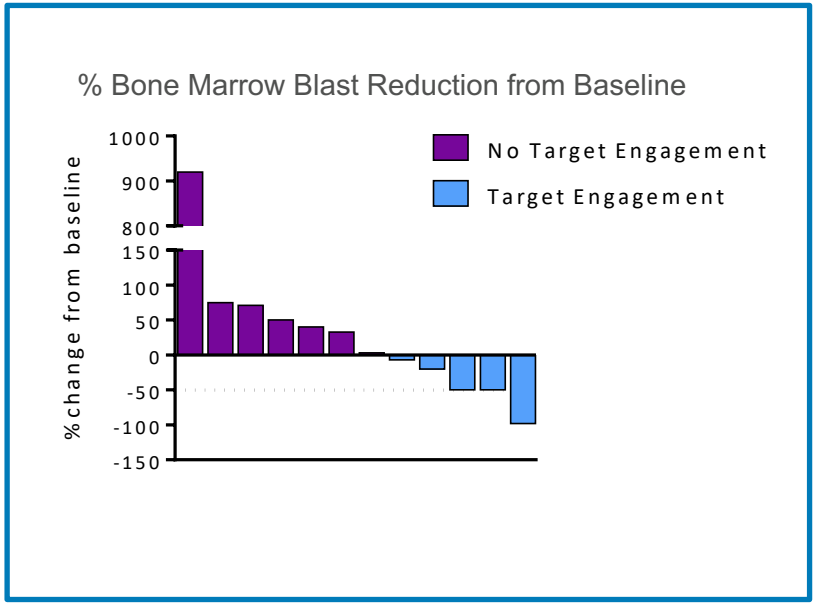
PLK1 Inhibition by Onvansertib is Correlated with Higher Response to Treatment[1]

- The 5 patients with target engagement showed a decrease in circulating blasts of ≥50% on the last time point recorded compared to baseline
- 3 of 5 patients with target engagement had a decrease of ≥50% in their last BM biopsy compared to baseline
- Decreases in circulating and bone marrow blasts were significantly higher in patients with target engagement compared to patients without target engagement





[3] American Society of Hematology (ASH) Conference Poster Presentation - December 2018

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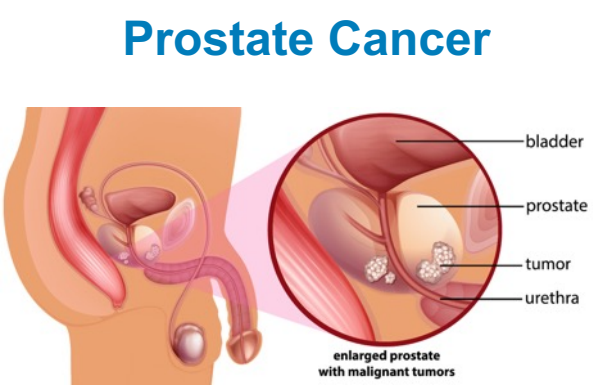
Metastatic Castration-Resistant Prostate Cancer
Opportunity to Increase Duration of Response to Therapy

- 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 months[4] 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 pathway[3,4]



[1]2017 Annual Report on Prostate Disease – Harvard Health Publications; [2]GlobalData. Prostate Cancer—Global Drug Forecast and Market Analysis to 2023. Apr, 2015; [3] National Cancer Institute Metastatic cancer. Mar, 2013. Available at: http://www.cancer.gov/about-cancer/what-is-cancer/metastatic-fact-sheet; [4]GAntonarakis, Emmannel – Current Understanding of Resistance to Abiraterone and Enzalutamide in Advanced Prostate Cancer; Clinical Advances in Hematology & Oncology – May 2016 – Volume 14, Issue 5

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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	Duration	Evaluation
Onvansertib – 24 mg/m^2 Days 1-5 (21-Day Cycle) + Zytiga®/prednisone daily	4 Cycles = 12 Weeks	Disease Control based on PSA level

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

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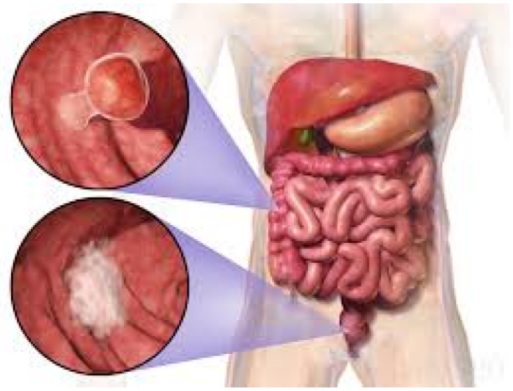
Colorectal Cancer: Unmet need in mCRC

- 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 1st 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)
  - 2nd line therapies have ~5% response rate in metastatic CRC (mCRC)

Colorectal Cancer



[1]https://seer.cancer.gov/statfacts/html/colorect.html; [2]King et al, Frontline Strategies for Metastatic CRC, 2016, Amer J Hem/Onc; Loree&Kopetz, Recent Developments in treatment of mCRC, 2017, Ther Adv Med Onc;

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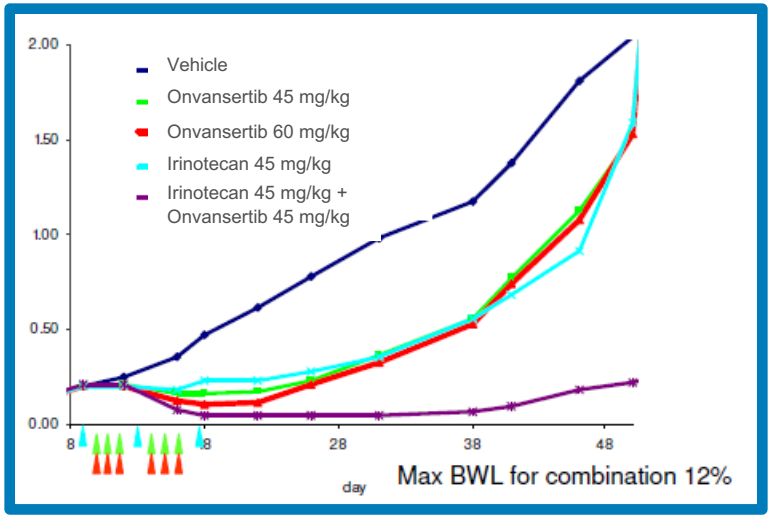
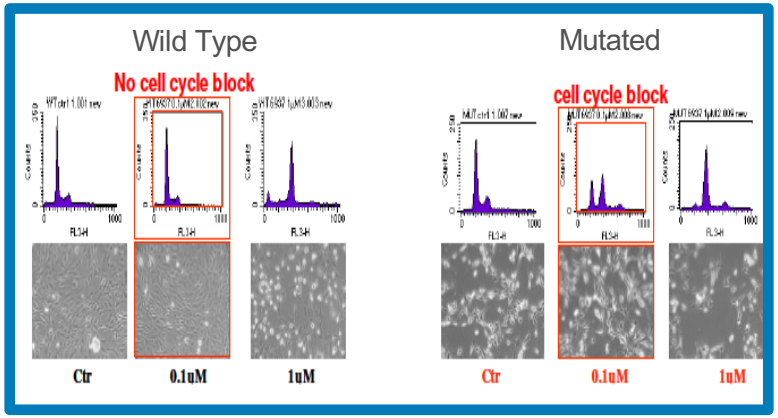
Onvansertib: Synergy in Combination with Irinotecan (FOLFIRI)

- 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

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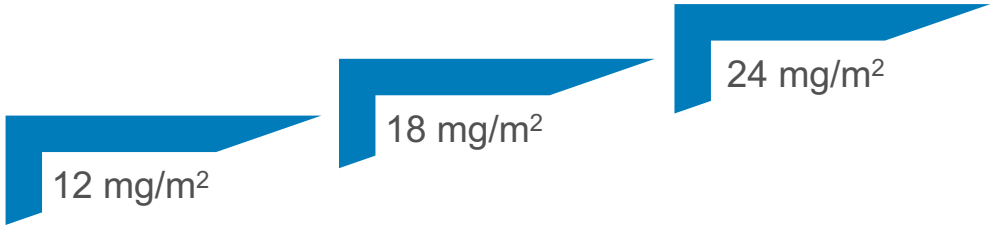
Planned Phase 1b/2 Clinical Trial in mCRC

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)

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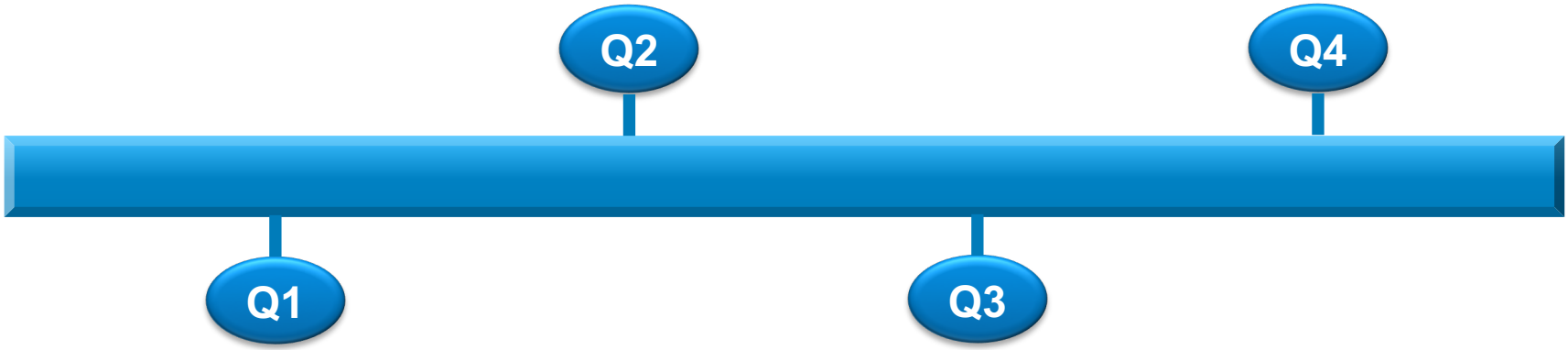
2019 Value Creating Milestones

- ✓ Initiate mCRC Phase 1b/2 trial
- ✓ Efficacy and safety data in AML, mCRPC
- ✓ AACR Presentations in AML, mCRPC
- ✓ Complete enrollment of AML Phase 2
- ✓ Complete enrollment of mCRPC Phase 2
- ✓ AML Companion Diagnostic

- ✓ Data Readouts (AML, mCRPC, mCRC)
- ✓ Begin Enrolling Phase 2 mCRC
- ✓ AML – ASH Presentation



- ✓ AML identify recommended Phase 2 dose (RP2D)
- ✓ Begin enrolling AML Phase 2 trial
- ✓ mCRPC ASCO-GU Presentation
- ✓ Efficacy and safety data readouts (AML and mCRPC)
- ✓ Formalize Japan Partnering Collaboration

- ✓ Efficacy and safety data readouts (AML and mCRPC)
- ✓ Assess dose escalation Phase 1b mCRC trial and identify Phase 2 dose

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