Transforming Oncology With Precision Cancer Therapeutics

trovagene

COMPANY OVERVIEW | JUNE 2017

Forward-Looking Statements

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About Trovagene

- Precision medicine biotechnology company developing therapeutics to improve cancer care by leveraging our proprietary Precision Cancer Monitoring® (PCM) technology in tumor genomics
  - Industry leader in urine and blood based tumor genomic diagnostics
  - Broad intellectual property and proprietary technology to measure, with high clinical sensitivities, circulating tumor DNA (ctDNA) in urine and blood for predicting response to cancer therapeutics
  - CLIA/CAP-accredited laboratory for internal drug development programs
- First therapeutic candidate: PCM-075, a polo-like kinase 1 (PLK1) inhibitor
  - Phase 1 completed with planned clinical development in AML
- NASDAQ listed: TROV

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Trovagene Product Pipeline

Therapeutics

CANDIDATE	DEVELOPMENT STAGE				
	R&D	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
PCM-075 Acute Myeloid Leukemia (AML)					
PCM-075 Safety / Solid Tumors					
PCM-075 Other Cancers					

Diagnostics

CANDIDATE	DEVELOPMENT STAGE		
	R&D	VALIDATION	MARKETED
Trovera™ EGFR, KRAS, BRAF NSCLC, CRC, Melanoma, Pancreatic			
NextCollect™ (RUO) urine collection and DNA preservation			
AML / PCM-075 Gene Panel			

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PCM-075: A PLK1 Inhibitor

- PCM-075 is an oral, highly-selective polo-like kinase 1 (PLK1) inhibitor
  - Licensed exclusive global development and commercialization rights from Nerviano Medical Sciences, S.r.l.
- Nerviano Medical Sciences: largest oncology-focused R&D company in Italy, highly regarded in Europe
  - Other licensees include: Genentech (Roche), Pfizer, Array Pharmaceuticals, Servier, Ignyta, and other biotechnology companies
- Trovagene's expertise in tumor genomic diagnostics, broad patents and technology uniquely enables our precision medicine approach in AML
  - Many core genomic markers covered in ctDNA PCM technology, including NPM1, a founder genetic marker in AML, for diagnosis and monitoring of patient response
  - Trovagene to optimize AML biomarker panel for patient selection and response to PCM-075

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PCM-075 Licensing Terms

- Trovagene has exclusive global development and commercialization rights to PCM-075
- Nerviano receives:
  - Upfront payment of $2.0 million
  - Milestones
    - Development: Phase 3
    - Regulatory: NDA submission
    - Commercial Launch
  - Tiered royalty payments up to and over $1.0 billion
- Trovagene has all rights to manufacturing of bulk and finished goods
  - Nerviano is the current manufacturer and has bulk material produced and available for clinical trials

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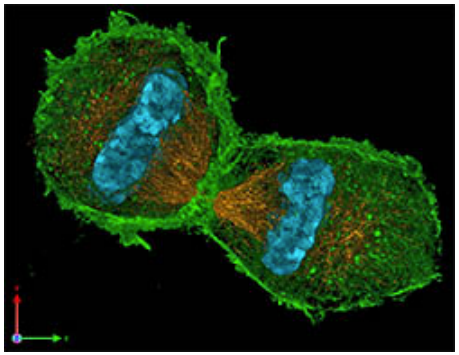
Polo-Like Kinase

- PLK1, PLK2, PLK3 are members of a family of serine/threonine kinases that are important regulators of cell-cycle progression[1–5]
- PLK1 is a master regulator of mitotic progression and is the only family member expressed exclusively in dividing cells[1–5]
- PLK1 regulates multiple steps of cell division[1–5]
  - Entry into mitosis
  - Centrosome maturation
  - Assembly of kinetochores and mitotic spindle
  - Cytokinesis and exit of mitosis
  - Role in genome stability during DNA replication



1. Takai N, et al. Oncogene 2005;24:287–91; 2. Rudolph D, et al. Clin Cancer Res 2009;15:3094–102; 3. Chopra P, et al. Expert Opin Investig Drugs 2010;10:27–43; 4. Strebhardt K. Nat Rev Drug Discov 2010;9643–60; 5. Zitouni S, et al. Nat Rev Mol Cell Biol 2014;15:433–52; 6. Takaki T, et al. Curr Opin Cell Bio 2008;20:650–60.

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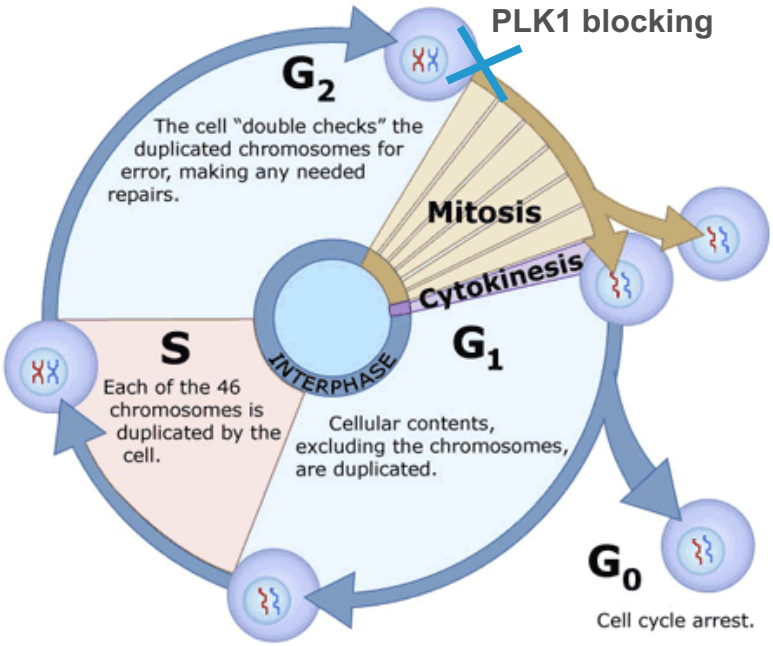
PLK1 As a Cancer Target

Inhibition of PLK1 Results in Cell Death[1]



Overexpression of PLK1 Observed in Numerous Cancer Types[2]

Table 1. Comparison of *PLK1* Expression between Cancers and Normal Tissue

Cancer Type	Full Name	*P* Value	Fold Change*
LUSC	Lung squamous cell carcinoma	7.41E-157	20.8
BRCA	Breast invasive carcinoma	5.88E-126	11.3
LUAD	Lung adenocarcinoma	1.18E-63	9.7
KIRC	Kidney renal clear cell carcinoma	2.33E-55	6.1
HNSC	Head and neck squamous cell carcinoma	6.52E-50	4.2
LIHC	Liver hepatocellular carcinoma	3.59E-40	11.7
UCEC	Uterine corpus endometrial carcinoma	1.96E-36	21.3
COAD	Colon adenocarcinoma	5.97E-33	2.5
STAD	Stomach adenocarcinoma	8.45E-27	4.8
ESCA	Esophageal carcinoma	9.52E-27	10.2
BLCA	Bladder urothelial carcinoma	4.96E-26	9.1
PRAD	Prostate adenocarcinoma	1.29E-22	3.3
KIRP	Kidney renal papillary cell carcinoma	6.76E-22	4.7
CHOL	Cholangiocarcinoma	6.97E-14	24.3
GBM	Glioblastoma multiforme	5.63E-12	12.4
KICH	Kidney chromophobe	1.63E-06	3.3
READ	Rectum adenocarcinoma	1.06E-05	2.3
PAAD	Pancreatic adenocarcinoma	0.04	2.2

* Mean *PLK1* expression in cancers/mean *PLK1* expression in normal tissue.

[1]Nature Reviews Molecular Cell Biology; [2]Translational Oncology, Feb 2017

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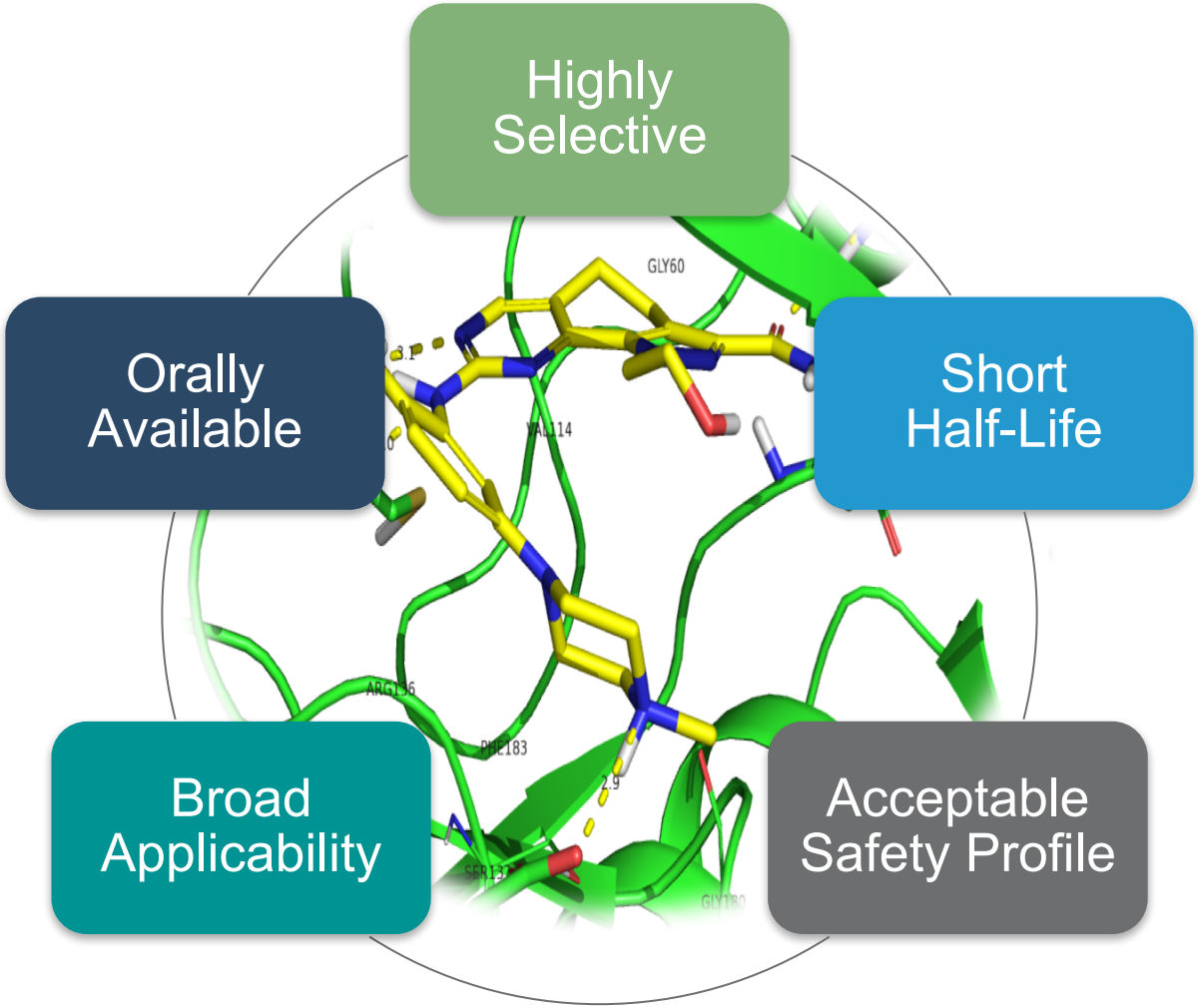
PCM-075 Attributes



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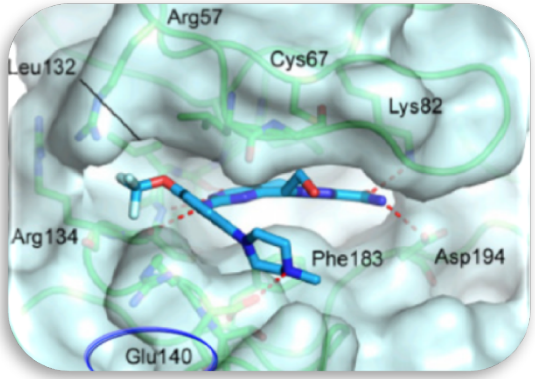
PCM-075 Biochemical Profile

Polo-like kinase 1 (PLK1) inhibitor

- Selective, adenosine triphosphate (ATP) competitive PLK1 inhibitor
- Selectivity driven by polar interaction with the carboxyl side chain of Glutamate 140 position of PLK1



PLK Member	PCM-075 IC50* (μM)
PLK1	0.002
PLK2	> 10
PLK3	> 10

* IC50 is the half-maximal concentration at which PCM-075 inhibits enzymatic activity

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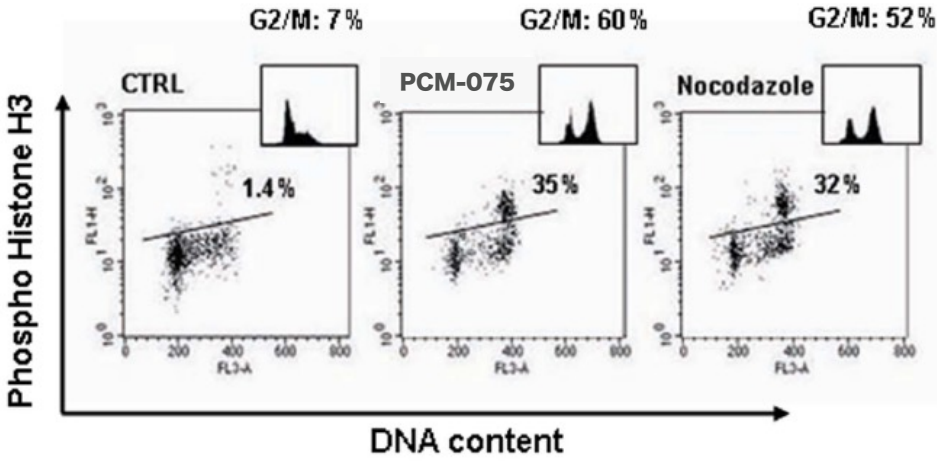
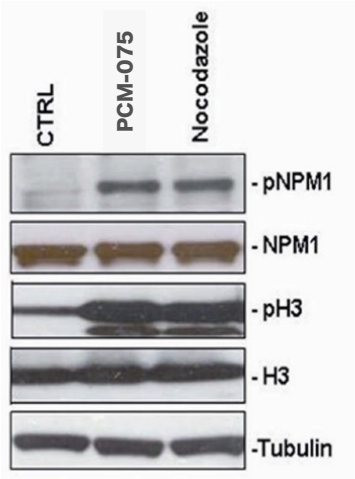
PCM-075 Mechanism of Action

Mitotic inhibitor demonstrating anti-proliferative activity*

- Induces a cellular phenotype of G2/M, leading to cell death
- Clear evidence of in-vitro pathway modulation in AML

AML-NS8 Patient-Derived Cells Treated with 200 nM PCM-075 for 24 Hrs[1]





* In numerous human cel lines; [1]Casolaro et al (2013) PLOS One

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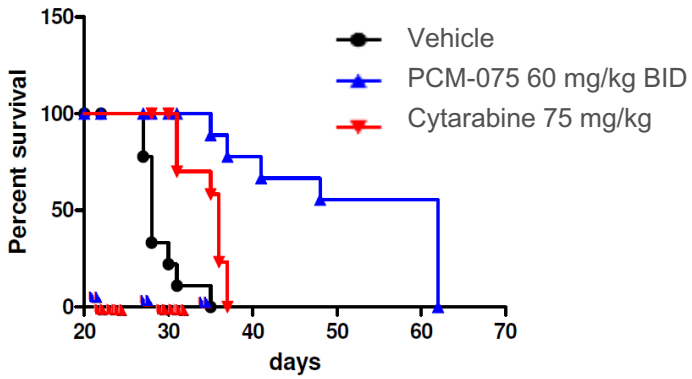
PCM-075 In-Vivo Activity

Response observed in various xenograft models as a single agent and in combination

In Vivo Disseminated Leukemia Model (AML-NS8 Cells)
Treatment with PCM-075 Started 20 Days Post-Inoculation
60 mg/kg BID (Days 1 and 2, 3 Cycles)



Compound	Median Survival Time (days)	%TGI
Placebo	28	
Cytarabine	38	128.6
PCM-075	62	221.4

Casolaro et al (2013) PLOS One

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PLK Inhibition in AML

Clinical activity published on PLK inhibitors

- Pan-PLK inhibitor demonstrated increased response rates, improvements in event-free survival, and overall survival benefit in combination with low-dose cytarabine (LDAC)
  - Adverse events observed in Phase 3 study, potentially due to drug accumulation and pan-PLKi activity
- Opportunity for a more selective PLKi with less drug accumulation paired with a precision medicine diagnostic

Compound	Selectivity	Half-Life (hrs)	Dosing	Clinical Activity in AML
Volasertib	pan-PLK	135	iv	25-30% CR+CRi (+LDAC)*
PCM-075	PLK1	24	oral	P1/2

* higher incidence of severe adverse events with volasertib plus LDAC in phase III study

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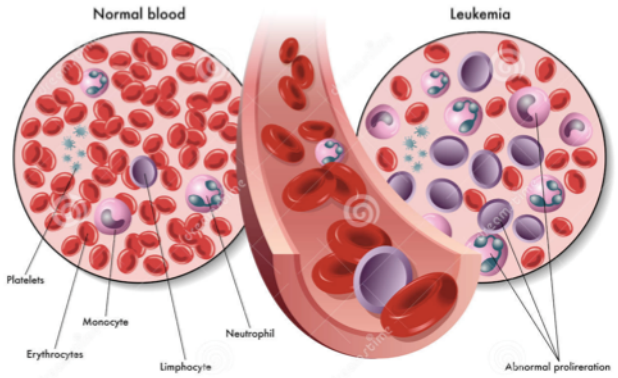
AML Market Opportunity

- AML: aggressive hematologic malignancy
- Incidence: 20,000 new cases and 10,400 deaths annually in the U.S.
- Prognosis: 5 year survival rate is 25%
- Treatment options vary based on patient condition / age, but can include:
  - Chemotherapy
  - Radiation
  - Stem cell transplant
- Genetic landscape includes:
  - NPM1, genetic marker in leukemia, accounting for ~ 30% of all AML patients
  - Other significant markers such as FLT3, DNMT3A, NRAS, KIT and fusion markers



National Cancer Institute SEER 2016

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Phase 1 study of PCM-075*

- Open-label, dose-escalation trial in patients with advanced or metastatic solid tumors
  - Enrolled 21 patients with confirmed metastatic disease and 62.7 years mean age
  - Patients received study medication at doses up to 48 mg/m2/day
- PCM-075 was administered orally, once daily for five consecutive days, every day for three weeks, to evaluate drug metabolism and first cycle dose-limiting toxicities (DLTs) and related maximum tolerated dose (MTD)
  - Also evaluated PCM-075's pharmacokinetic profile in plasma, its anti-tumor activity, and its ability to modulate intracellular targets in biopsied tissue
- Reversible thrombocytopenia and neutropenia were identified as the primary DLTs, which are consistent with the expected mechanism of action and results from preclinical studies.
  - One patient experienced grade 3 constipation, which may have been due to concomitant treatment with opiates; no other clinically relevant safety findings emerged

*Manuscript submitted for publication

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PCM-075 Clinical Development Plan

- Active IND for PCM-075 with clinical and regulatory organization engaged
- Phase 1/2 study planned with enrollment in 2017
  - Dose-escalation with PCM-075 as single agent and then in combination with chemotherapy agents to assess patient response and explore use of correlative biomarkers to select patients most likely to respond
  - Inclusion criteria: adults with previously untreated AML, ineligible for intensive therapy, and ECOG 0-2
- Clinical Advisory Board
  - Dr. Jorge Cortes, MD Anderson Cancer Center (Deputy Chair Leukemia)
  - Dr. Sandra Silberman, Duke
  - Dr. Filip Janku, MD Anderson Cancer Center
  - Dr. David Berz, Beverly Hills Cancer Center

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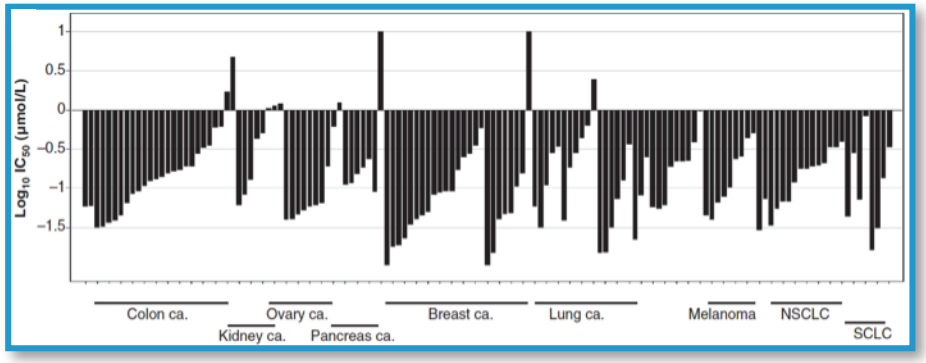
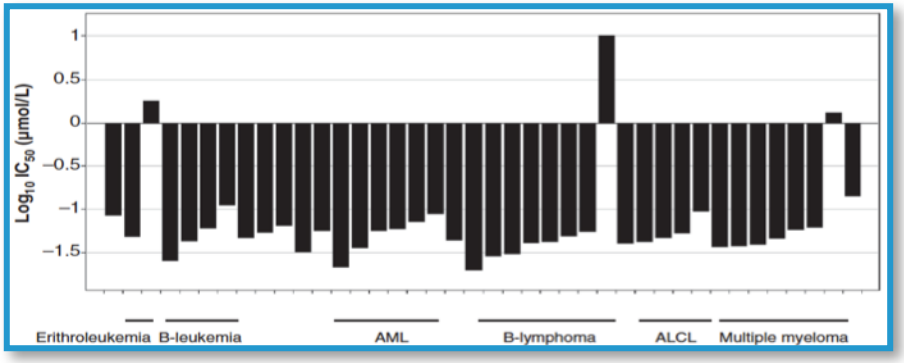
PCM-075: Broad Clinical Opportunities

- Extensive preclinical data supportive of:
  - Hematologic cancers (leukemias and lymphomas)
  - Solid tumor cancers (breast, colon, ovarian, lung)

IC_{50} values for inhibition of cell proliferation after treatment with PCM-075 in a panel of cell lines derived from solid tumors



IC_{50} values for inhibition of cell proliferation after treatment with PCM-075 in a panel of cell lines derived from hematologic tumors



Mol Cancer Ther; 11(4) April 2012

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Trovagene ctDNA PCM Technology

- Proprietary ctDNA technology allows us to uniquely measure, with high clinical sensitivity, circulating genetic fragments of cancer tumors
  - Over 120 patents issued and 60 pending
- Only liquid biopsy company with ctDNA technology compatible in both urine and blood for predicting patient response to therapeutics
- Trovera® single gene assays: CLIA and clinically validated tests for lung, colorectal, pancreatic, melanoma, other cancer types, and histiocytic disorders
  - ERTHOS™ Select multigene panel with >200 mutations for broad applications, under development

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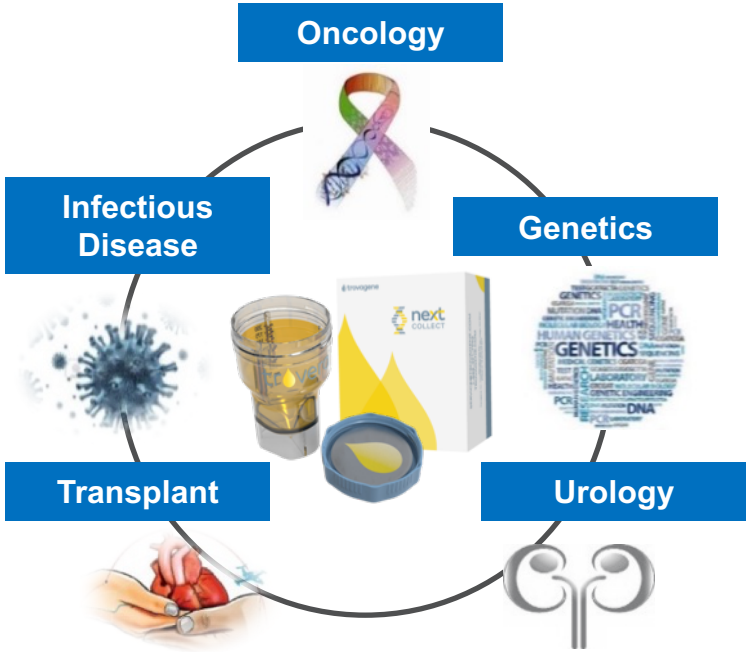
NextCollect™

Urine collection and DNA preservation system

- First of its kind urine collection and DNA preservation system
- Comprehensive analysis of cell-free and cellular DNA
- Research use only (RUO)
- Opportunity for global distribution



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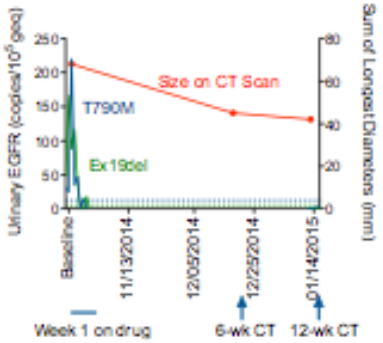
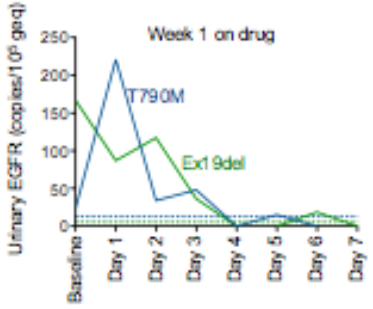
Monitoring of Cancer
concordant with radiographic response

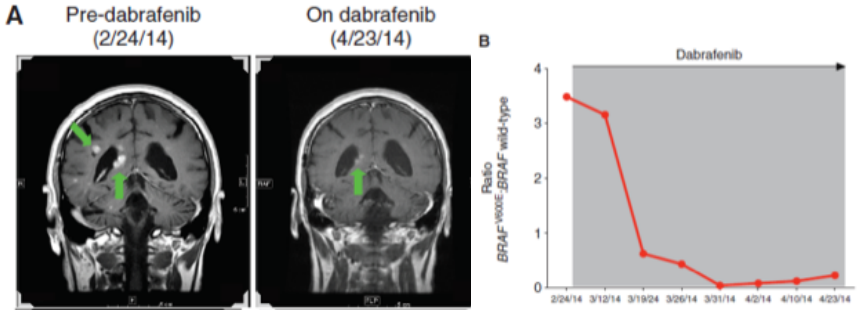
Trovagene's ctDNA tests can be effectively used to monitor therapeutic response

NSCLC 3rd Generation TKI/*EGFR* T790M[1]





Histiocytic Tumor/*BRAF* Inhibitor[2]



[1] Multiple peer-reviewed studies including Husain, Kurzrock et al, World Lung Conference, 2015; [2]Hyman et al., Cancer Discovery 2015; [3]Klempner et al., Cancer Discovery 2016

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AML Biomarker Strategy

- Trovagene to develop AML biomarker panel for clinical study
  - NPM1 patent for diagnosis and monitoring of patient response owned by Trovagene
  - Most other markers already assessed with ctDNA PCM technology
  - Patient selection pre and post response to therapy

Gene	Overall Frequency (%)
FLT3 (ITD, TKD)	37 (30, 7)
NPM1	29
DNMT3A	23
NRAS	10
CEBPA	9
TET2	8
WT1	8
IDH2	8
IDH1	7
KIT	6
RUNX1	5
MLL-PTD	5
ASXL1	3
PHF6	3
KRAS	2
PTEN	2
TP53	2
HRAS	0
EZH2	0

Patel J, et al. Prognostic relevance of integrated genetic profiling in acute myeloid leukemia. N Engl J Med. 2012;366:1079-89

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Select Upcoming Milestones

- Phase 1/2 clinical trial protocol for PCM-075 in patients with AML
- Publication of PCM-075 phase 1 safety study in solid tumors
- Presentation of preclinical data in AML, other hematologic cancers and solid tumor cancers at key conferences
- Development of an AML genetic marker panel
- Announcement of phase 1 and phase 2 clinical sites and enrollment of patients
- Execution of commercial development programs including clinical testing services, licensing and research kit sales

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Summary

- PCM-075
  - Oral and highly-selective PLK1 inhibitor
  - Favorable 24-hour half-life for AML treatment therapy with reversible hematologic toxicities
  - Phase 1/2 trial in AML
- PCM diagnostic technology
  - Development of PCM-075 AML biomarker panel
  - Launch NextCollect™
  - Pharma lab services collaborations

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Thank you

for more information, please email ir@trovagene.com