Reimagining Cancer Treatment

Syndax

Determined to realize a future in which people with cancer live longer and better than ever before

Cantor Fitzgerald 2nd Annual Healthcare Conference •
July 13, 2016

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Company Strategy

Entinostat Breast Cancer

Entinostat Immuno-oncology

New molecules

Financing & Staffing

With an expected IND filing in 2016, two potential best-in-class molecules in clinical studies

		Preclin	Ph 1	Ph 2	Ph 3	Indication
Entinostat (HDAC inhibitor)	Ph 3 trial in combination with hormone therapy					HR+ MBC
	Three trials exploring five PoC indications in combination with PD(L)-1 antibodies					NSCLC, melanoma, TNBC, ovarian
	Multiple IST/NCI sponsored trials testing immunoncology combos					Solid tumors
SNDX-6352 (Anti-CSF-1R)	Trials initiating 4Q2016					Solid tumors

HR+ MBC = hormone receptor positive metastatic breast cancer; NSCLC = non-small cell lung cancer; TNBC = triple negative breast cancer; IST = investigator sponsored trial; NCI = National Cancer Institute

Company Strategy

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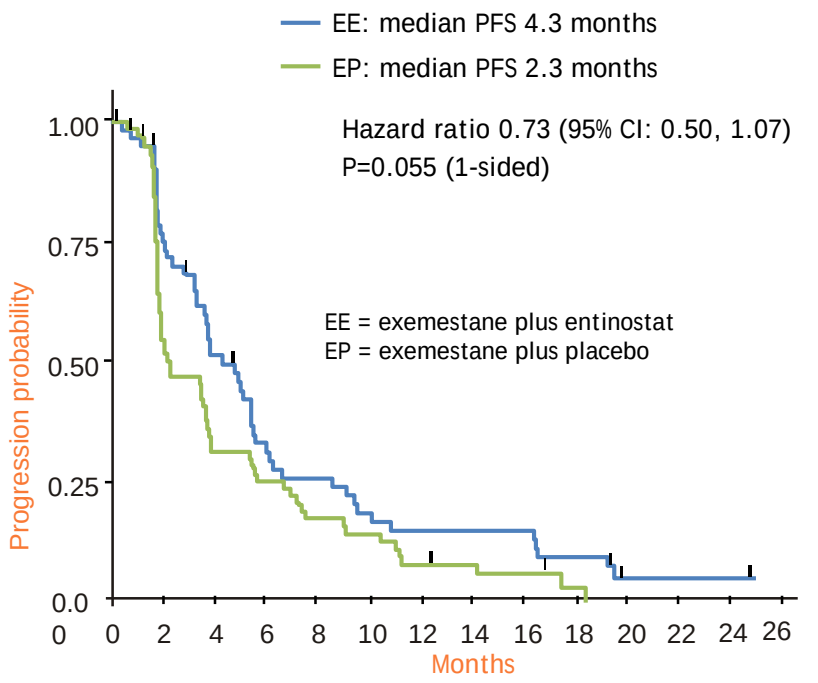
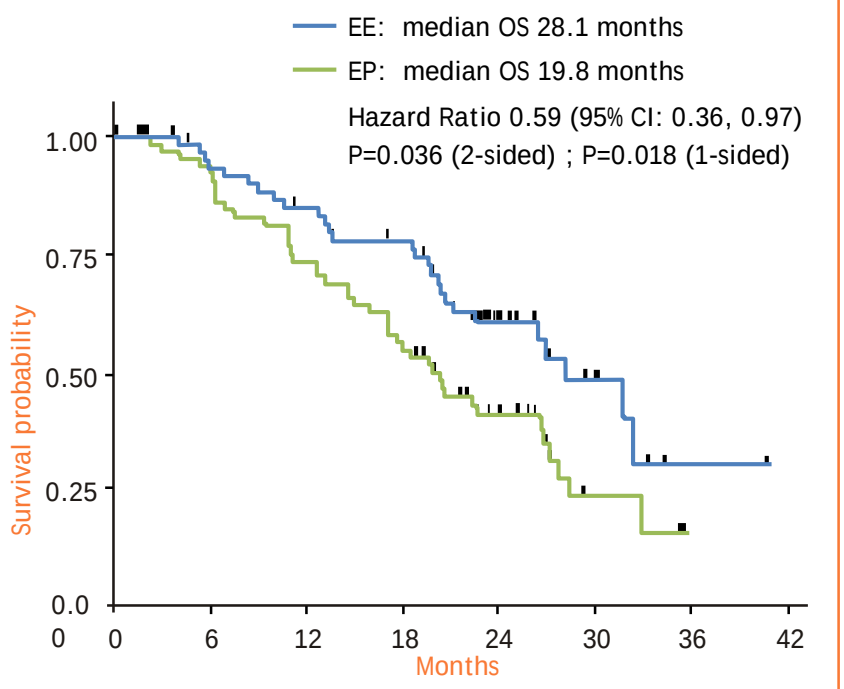
Phase 2 trial resulted in breakthrough therapy designation for entinostat + exemestane in advanced HR+ breast cancer

Progression-Free Survival



Overall Survival



Source: Yardley, Denise A., et al. Journal of Clinical Oncology 31.17 (2013): 2128-2135.

Entinostat-exemestane combination is generally well tolerated

Adverse Event[a]	Exemestane + Entinostat (N=63)			Exemestane + Placebo (N=66)		
	Any Grade (G) n (%)	G3 n (%)	G4 n (%)	Any Grade (G) n (%)	G3 n (%)	G4 n (%)
Fatigue	30 (48%)	7 (11%)	1 (2%)	17 (26%)	2 (3%)	–
Nausea	25 (40%)	3 (5%)	–	10 (15%)	1 (2%)	–
Neutropenia[b]	19 (30%)	8 (13%)	1 (2%)	–	–	–
Vomiting	13 (21%)	3 (5%)	–	3 (5%)	–	–
Headache	9 (14%)	3 (5%)	–	7 (11%)	–	–
Hypophosphataemia	4 (6%)	3 (5%)	–	3 (5%)	1 (2%)	–

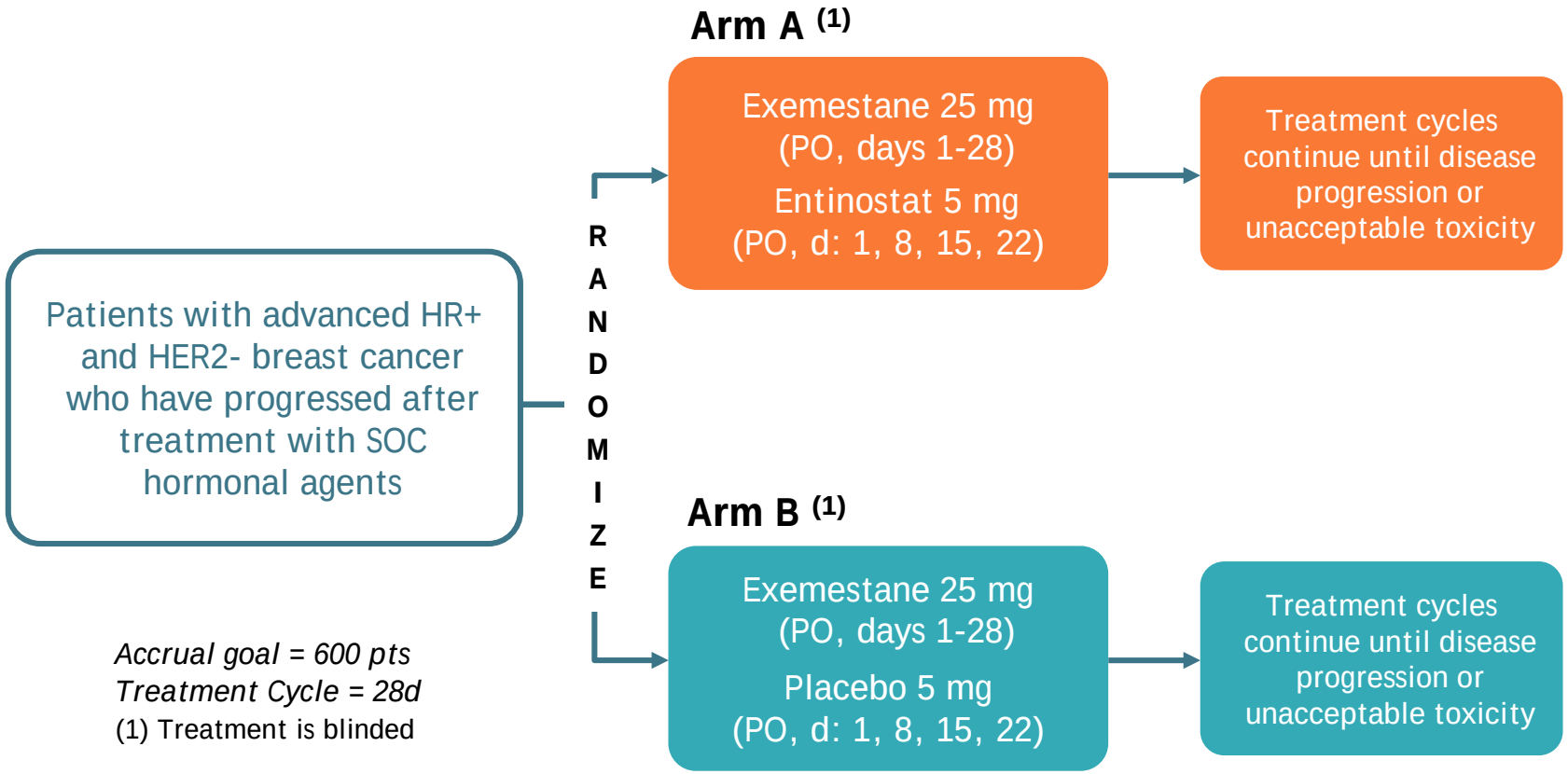
(a) Grade 3 and 4 AEs occurring in >5% in exemestane plus entinostat group; Safety Population; Treatment-emergent AEs, regardless of treatment-attribution

(b) None of these eight grade 3 and 4 patients experienced febrile neutropenia or associated infections during the time of the neutropenia. One patient with non-measurable bone-only disease was given a myeloid growth factor for neutrophil support; patient had history of neutropenia and growth factor usage.

Source: Yardley, Denise A., et al. *Journal of Clinical Oncology* 31.17 (2013): 2128-2135.

E2112, a Phase 3 registration trial in advanced HR+ breast cancer patients, is underway

E2112 Pivotal Trial Design



E2112 designed to show overall survival benefit

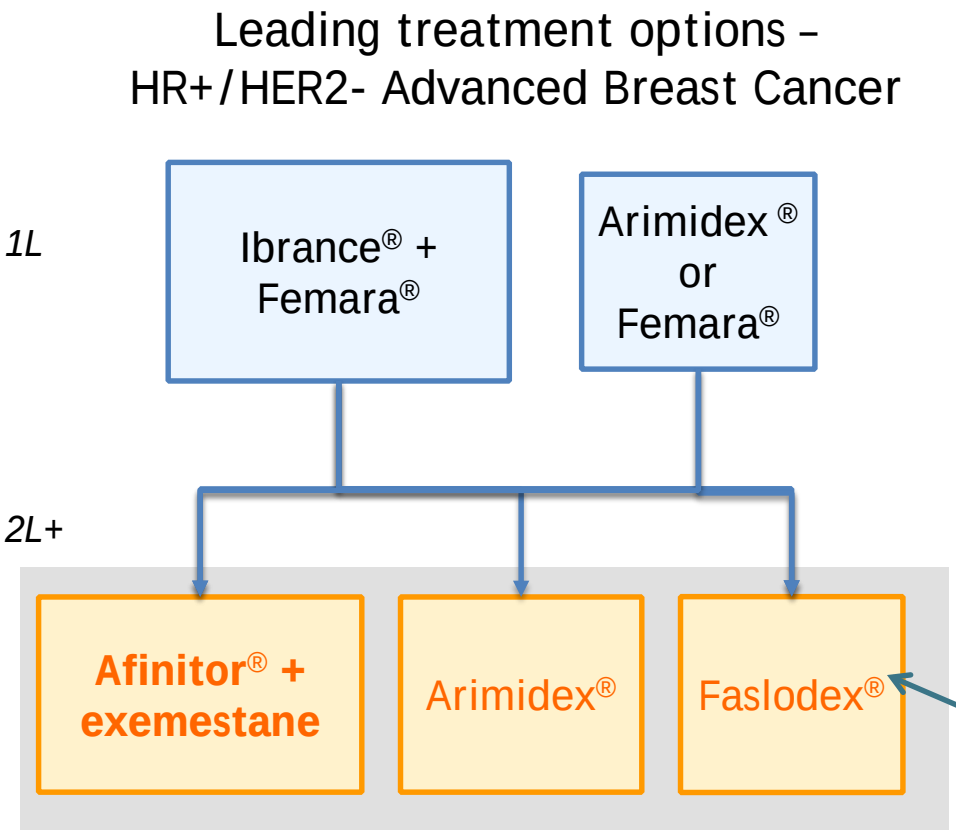
Trial Details

- Trial being conducted by ECOG-ACRIN* with NCI sponsorship
- FDA granted trial Special Protocol Assessment (SPA)
- Two primary endpoints: PFS and OS

ECOG-ACRIN reported enrollment has exceeded 200 patients and interest continues to build^

* ECOG-ACRIN = Eastern Cooperative Oncology Group-American College of Radiology Imaging Network Cancer Research Group
^ ECOG-ACRIN April Newsletter

Second-line HR+ metastatic breast cancer may represent a significant market opportunity

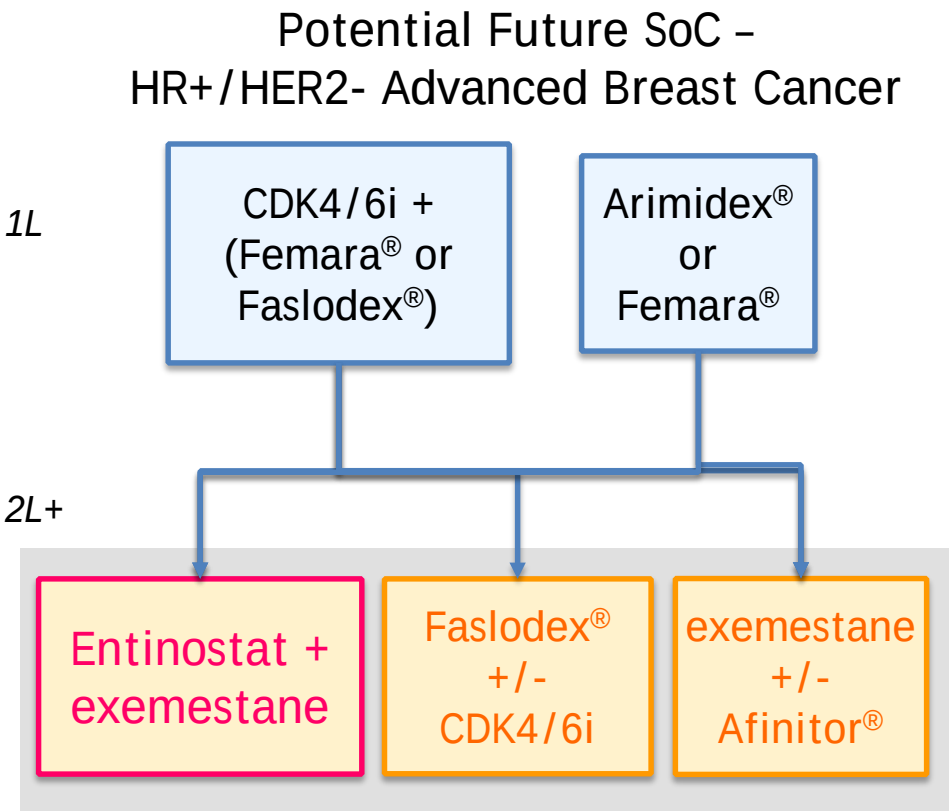


- CDK4/6 inhibitor Ibrance rapidly became a first-line (1L) standard-of-care (SoC)
- Afinitor + exemestane most common second-line (2L) combination despite toxicity and lack of an OS benefit

~34,000 patients receive hormone therapy[1] after 1st line

[1]*LEK estimate*
Source: DataMonitor 2016 Breast cancer: HR+/HER2- Disease Coverage Report

Entinostat could supplant Afinitor with a survival benefit



- Additional CDK4/6 inhibitors primarily compete in 1L
- Entinostat + exemestane likely becomes 2L SoC with positive OS

No other combination has shown an OS advantage over hormone therapy alone

Source: DataMonitor 2016 Breast cancer: HR+/HER2- Disease Coverage Report; Novartis 2Q15 earnings presentation

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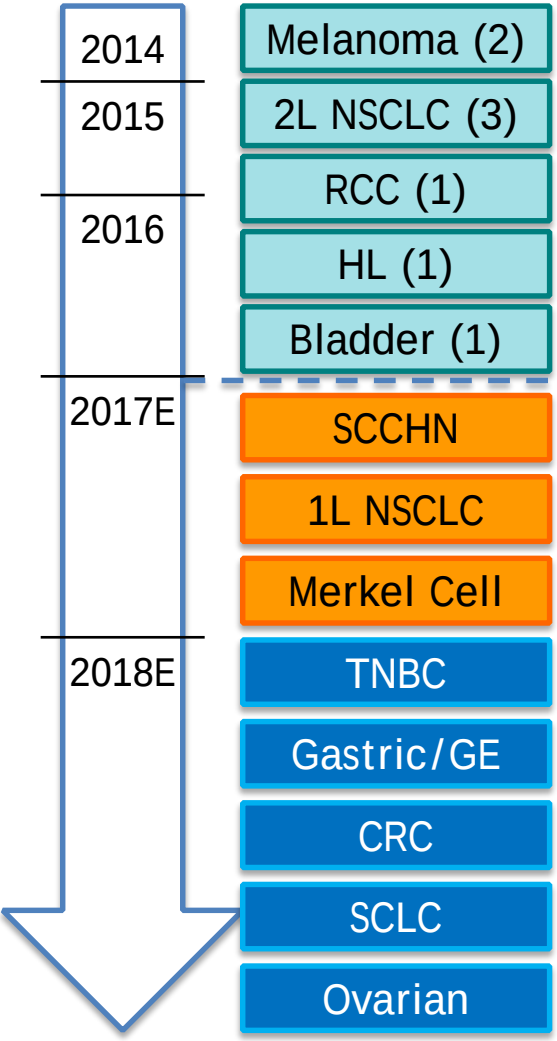
Immuno-Oncology (IO) is rapidly defining new therapeutic standards



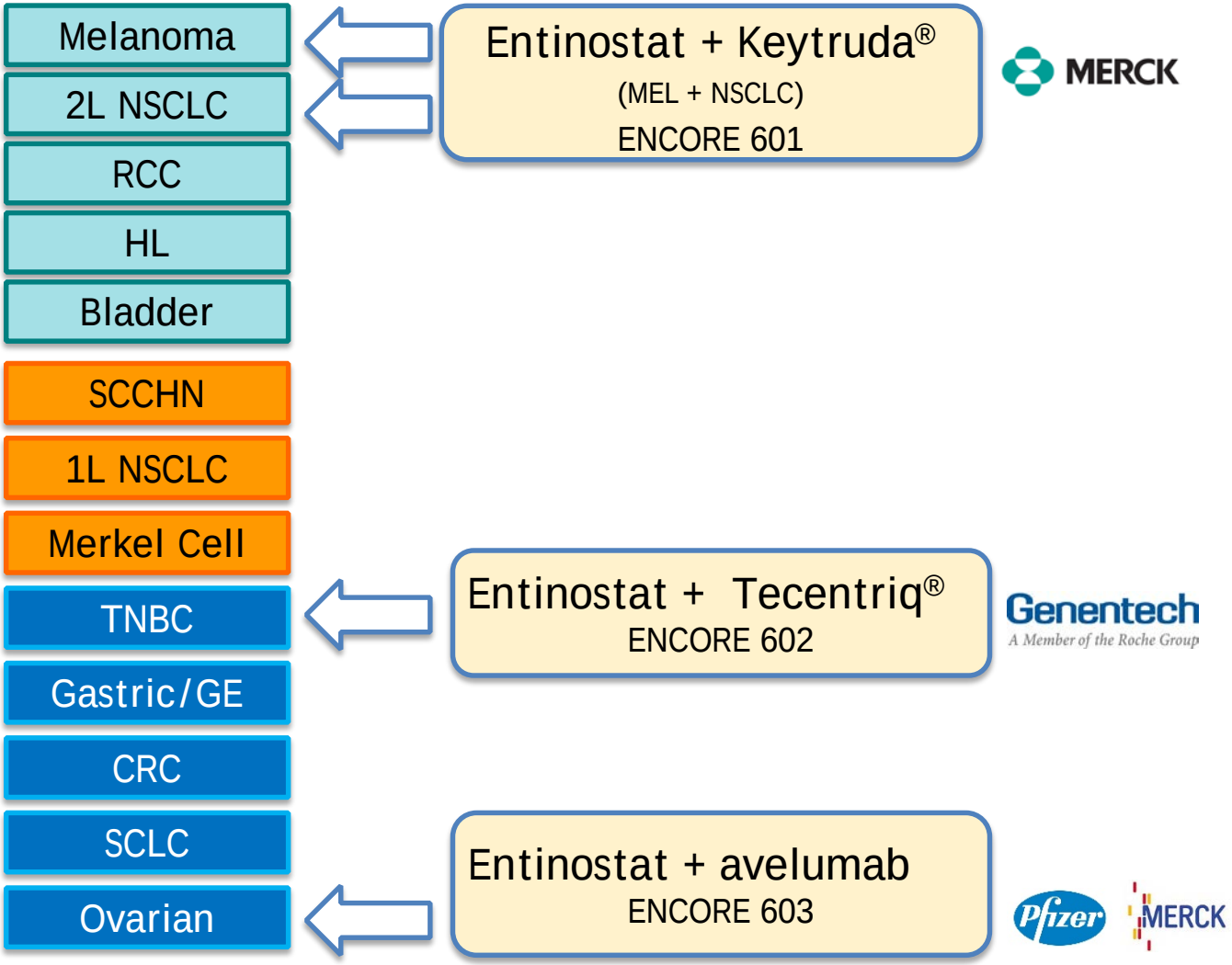
- **Since late 2014, three PD(L)-1inhibitors have received eight FDA approvals for five different tumors**

- **Recent data suggest additional approvals in 2017**
  - Head and neck: Opdivo trial stopped early
  - 1L PDL-1+ NSCLC: Positive PFS and OS for Keytruda
  - Merkel Cell: Avelumab filing with Phase 2 data

- **Phase 3 results expected in six new tumor types as well NSCLC and melanoma in 2017 and 2018**

Source: clinicaltrials.gov; company press releases

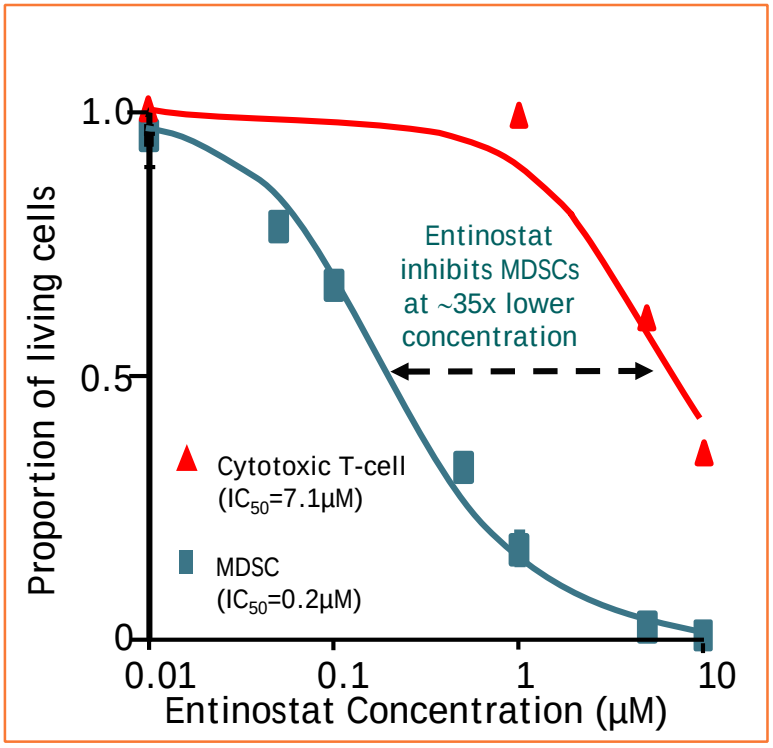
Potential near-term opportunity to demonstrate entinostat activity in combination

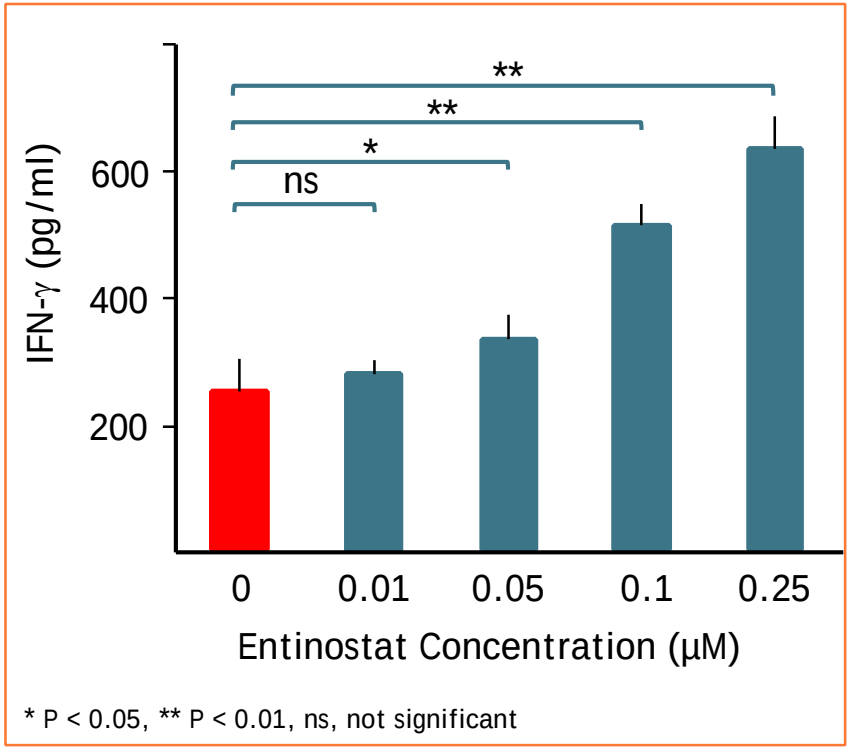


Eradication of metastatic mouse cancers resistant to immune checkpoint blockade by suppression of myeloid-derived cells

KiBem Kim[a], Andrew D. Skora[a], Zhaobo Li[a], Qiang Liu[a], Ada J. Tam[b], Richard L. Blosser[b], Luis A. Diaz, Jr.[a], Nickolas Papadopoulos[a], Kenneth W. Kinzler[a], Bert Vogelstein[a,c,1], and Shibin Zhou[a,1]

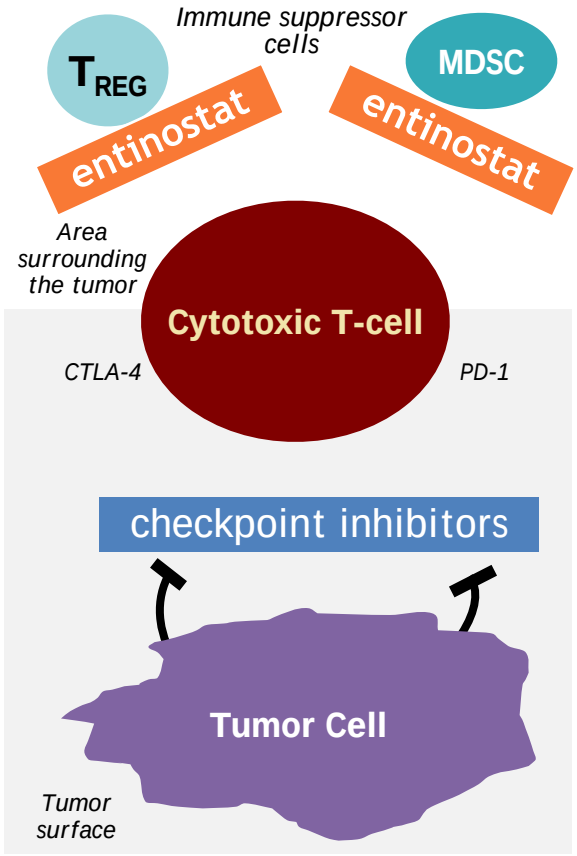
[a]Ludwig Center for Cancer Genetics and Therapeutics, Sidney Kimmel Comprehensive Cancer Center, [b]Oncology Flow Cytometry Core Facility, and [c]Howard Hughes Medical Institute, The Johns Hopkins University School of Medicine, Baltimore, MD 21287





PNAS 111.32 (2014): 11774-11779

Entinostat's differentiated mechanism targets immuno-suppressive tumor microenvironment

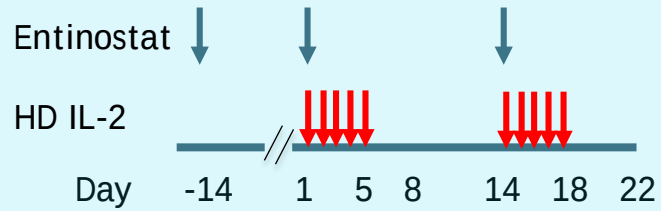


- **Entinostat inhibits the effect of two key immuno-suppressive cells:**
  - Myeloid derived suppressor cells **(MDSCs)**
  - T-Regulatory cells **(Tregs)**
- **Entinostat's targeting of immune suppressor cells synergizes with immune checkpoint blockade**

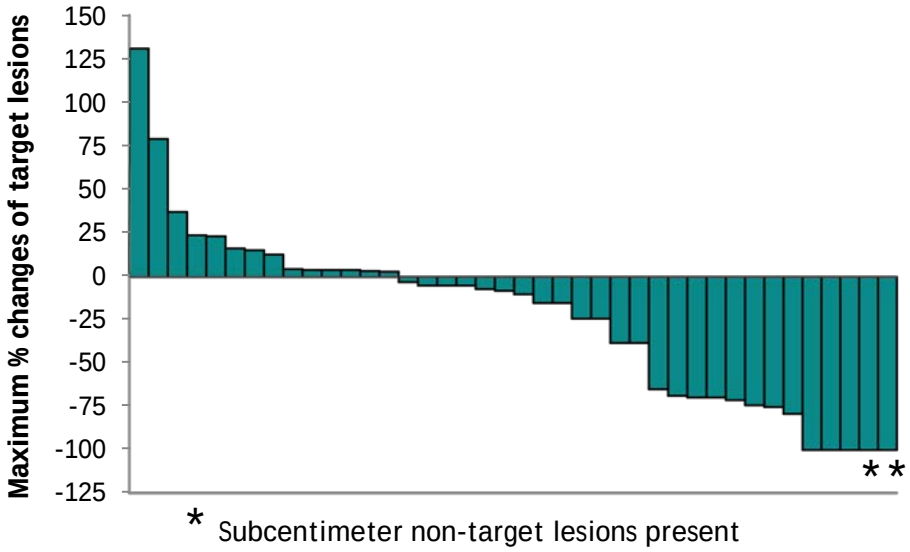
Entinostat may increase anti-tumor effect of high dose IL-2 by modulating immuno-suppressive cells

NCI-7870 Phase 1b/2 Entinostat + High Dose IL-2
in Metastatic Renal Cell Carcinoma

- Is response rate of combo greater than IL-2 alone? (ORR 20%)
- Dosing
  - Entinostat: 3 or 5 mg P.O.
  - HD IL-2: 600,000 U/kg Q8hr



- 41 patients evaluated



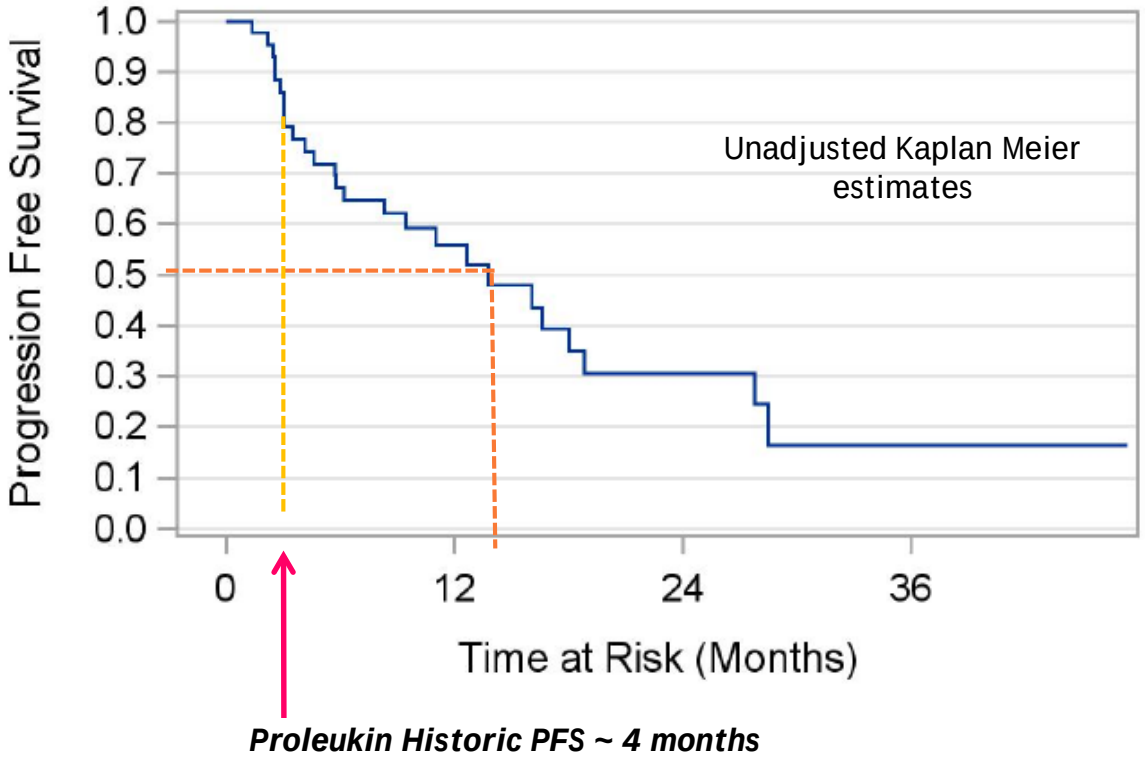
* Subcentimeter non-target lesions present

- Overall Response rate 37%
  (95% CI 22-53%)
- CR 7% (n = 3)
- PR 29% (n = 12)
- SD > 6 mos 22% (n = 9)

Source: Pili R et al ASCO 2016

Entinostat, IL-2 combination appears to substantially increase median PFS over IL-2 alone

Entinostat – Proleukin median PFS = 13.8 mos [95% CI 6.2,18.8]



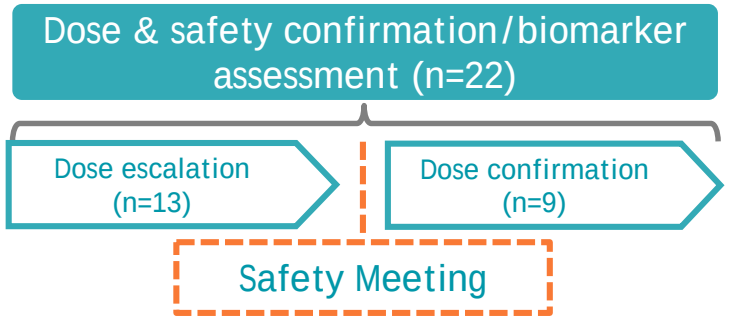
Source: Pili R et al ASCO 2016

ENCORE 601: First signal seeking study across 3 indications

KEYTRUDA® + Entinostat

MERCK

Phase 1b:
open-label



Phase 2:
Simon 2-stage, open-label

Stage 1	Stage 2	Total n
NSCLC - PD-(L)1 – naïve (n=13)	NSCLC - PD-(L)1 – naïve (n=33)	46
NSCLC - PD-(L)1 progressing (n=20)	NSCLC - PD-(L)1 progressing (n=36)	56
Melanoma PD-(L)1 progressing (n=13)	Melanoma PD-(L)1 progressing (n=21)	34

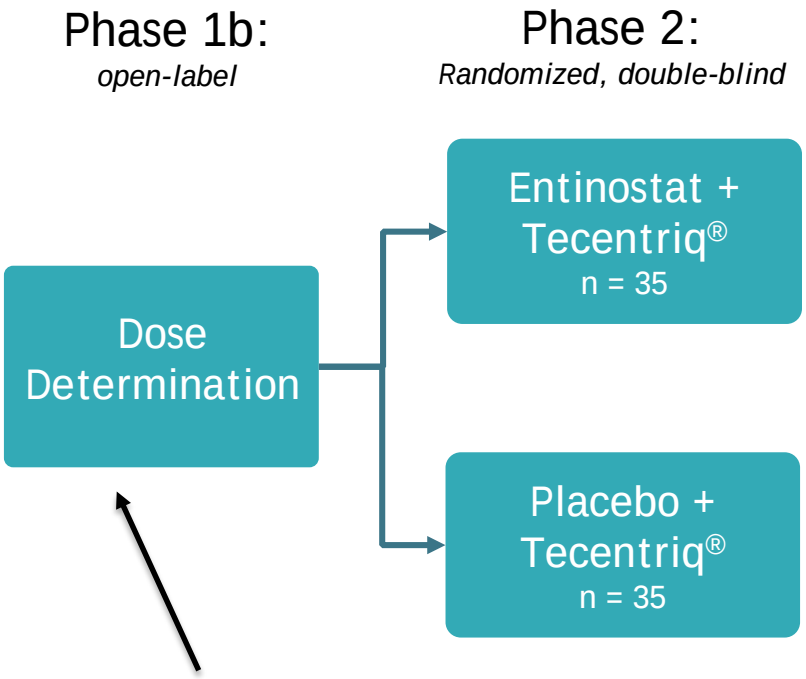
Study Milestones:

- Completed accrual for dose escalation stage
- Positive safety assessment made by DSMB
- Dose confirmation stage estimated completion in Q3-16
- Phase 1b data presentation anticipated 4Q16

ENCORE 602 is the result of our collaboration with another industry innovator

Genentech
A Member of the Roche Group

Triple Negative Breast Cancer



Phase 1b initiated in June 2016

Trial Centers

Primary: UCLA Health

CRO: Translational Research in Oncology Group **(TRIO)**

Primary Endpoints

- Phase 1b – Establish phase 2 dose
- Phase 2 – PFS using RECIST 1.1

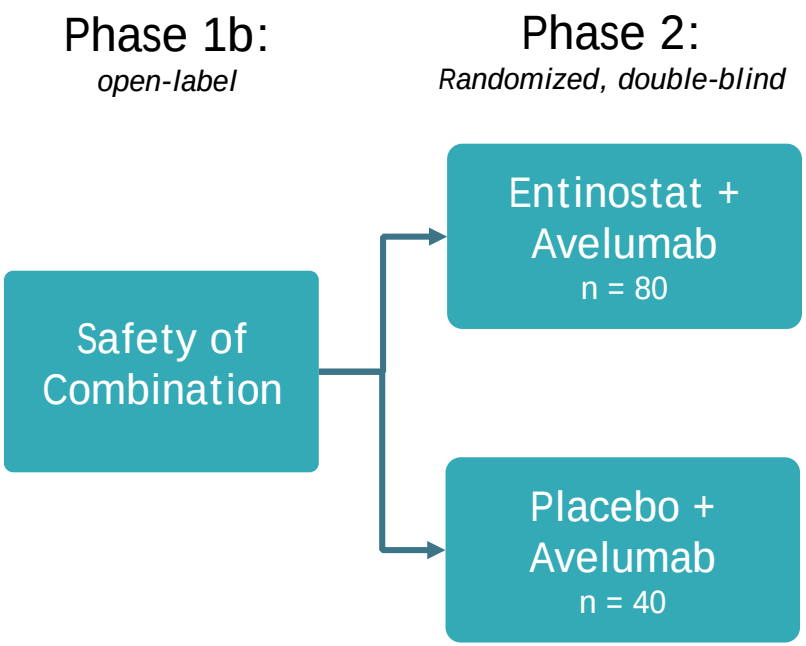
Secondary Endpoints

- ORR
- OS
- Safety & tolerability

ENCORE 603 seeks to demonstrate the breadth of entinostat efficacy

MERCK – Pfizer

Ovarian Cancer



Primary Endpoints

- Phase 1b – Establish safety of the combination
- Phase 2 – PFS using RECIST 1.1

Secondary Endpoints

- ORR
- OS
- Safety & tolerability

Phase 1b update: First patient is expected to be dosed during 4Q-16

ENCORE Clinical Trial Programs

- The ENCORE trials are designed to establish entinostat's ability to enhance checkpoint efficacy
- Entinostat-checkpoint inhibitor combination trials are expected to generate multiple milestones over the next 12 months

Entinostat-checkpoint combinations			Anticipated data presentation	
Trial	Partner	Indication	2H16	1H17
ENCORE 601	MERCK	NSCLC – PD(L)-1 naïve	Phase 1b RP2D	Phase 2; 1st Stage
		NSCLC – PD(L)-1 refractory		Phase 2; 1st Stage
		Melanoma		Phase 2; 1st Stage
ENCORE 602	Genentech A Member of the Roche Group	TNBC	Phase 1b safety, RP2D	
ENCORE 603	MERCK Pfizer	Ovarian		Phase 1b safety

RP2D = Recommended Phase 2 Dose

Company Strategy

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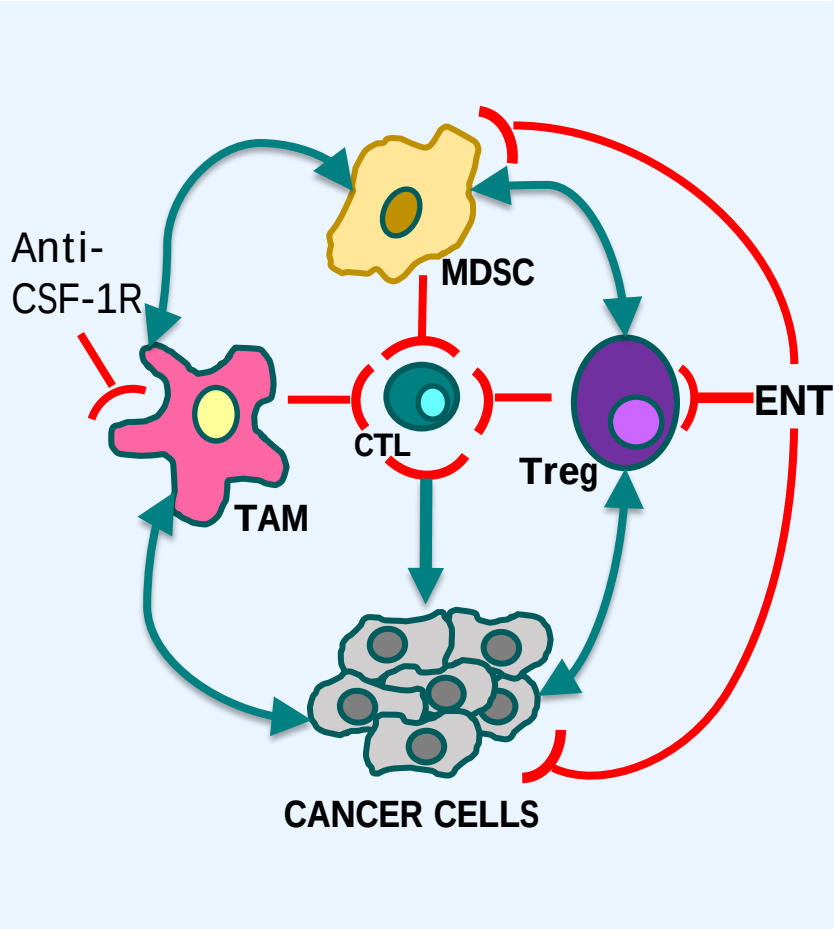
New molecules

Financing & Staffing

CSF-1R regulates proliferation, survival, differentiation, and chemotaxis of mononuclear phagocytes

- CSF-1R is expressed on mononuclear phagocytic cells, including immunosuppressive TAMs
- Anti-CSF-1R Ab depletes TAMs and increases tumor infiltrating lymphocytes
  - inhibition shows clinical activity in diffuse-type giant cell tumor
  - Preclinical synergistic anti-tumor activity seen with immune checkpoint inhibitors



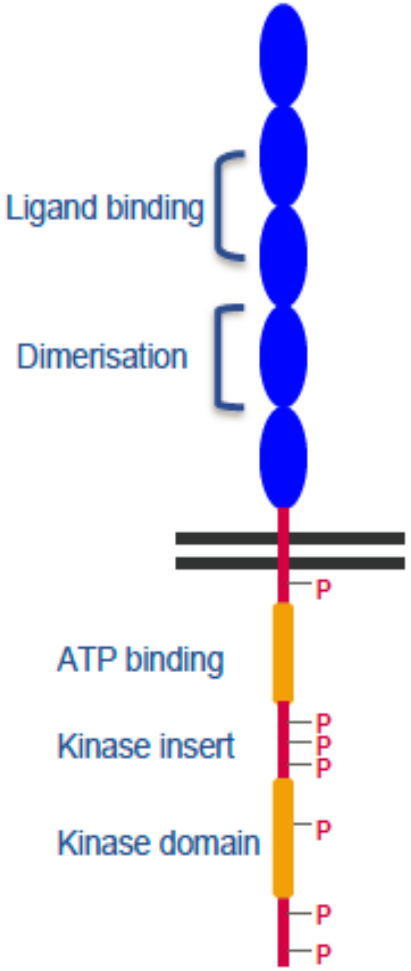
MDSC – myeloid derived suppressor cell; TAM – tumor associated macrophage; Treg – regulatory T lymphocyte; CTL – cytotoxic T cell; ENT – entinostat; CSF-1R – colony stimulating factor -1 receptor

Source: data on file

Syndax anti-CSF-1R antibody properties

- SNDX-6352, developed at UCB as UCB6352
- High affinity, humanized IgG4P (K_D = 4-8 pM)
- Demonstrated binding to ligand binding domain; blocks CSF-1 and IL-34 binding
- Inhibits ligand induced monocyte activation
- No evidence of antibody mediated receptor internalization or activation
- IND-enabling studies completed by UCB

SNDX-6352



Source: data on file

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Anticipated Syndax data announcements

Timing	Study	Indication	Phase	Milestone	Sponsor/Study #
2H16	Entinostat + KEYTRUDA®	NSCLC	1b	RP2D	Syndax/ENCORE 601
	Entinostat + Tecentriq®	TNBC	1b	Safety	Syndax/ENCORE 602
1H17	Entinostat + KEYTRUDA®	NSCLC, MEL	2	Go/No Go 1st Stage	Syndax/ENCORE 601
	Entinostat + avelumab	Ovarian	1b	Safety	Syndax/ENCORE 603
	SNDX-6352	Solid Tumors	1	SAD	Syndax/TBD
2H17	Entinostat + *exemestane*	HR+ BC	3	PFS data	NCI/E2112 (Syndax)
	Entinostat + avelumab	Ovarian	1b	RP2D	Syndax/ENCORE 603
	SNDX-6352	Solid Tumors	1	MAD	Syndax/TBD

Cash expected to fund key milestones into mid-2018

Milestones Anticipated

- Achieve PFS endpoint in entinostat Phase 3 clinical trial in advanced HR+ Breast Cancer
  - File NDA for entinostat in HR+ Breast Cancer
- Complete Phase 1b/2 IO-entinostat combination trials with:
  - KEYTRUDA® (pembrolizumab)
  - Tecentriq® (atezolizumab)
  - Avelumab
- Complete SNDX-6352 Phase 1 program

Cash balance as of 3/31/16: $133.7M[1]

[1] *Includes cash, cash equivalents and short-term investments*

Thank you. Questions?

Syndax