

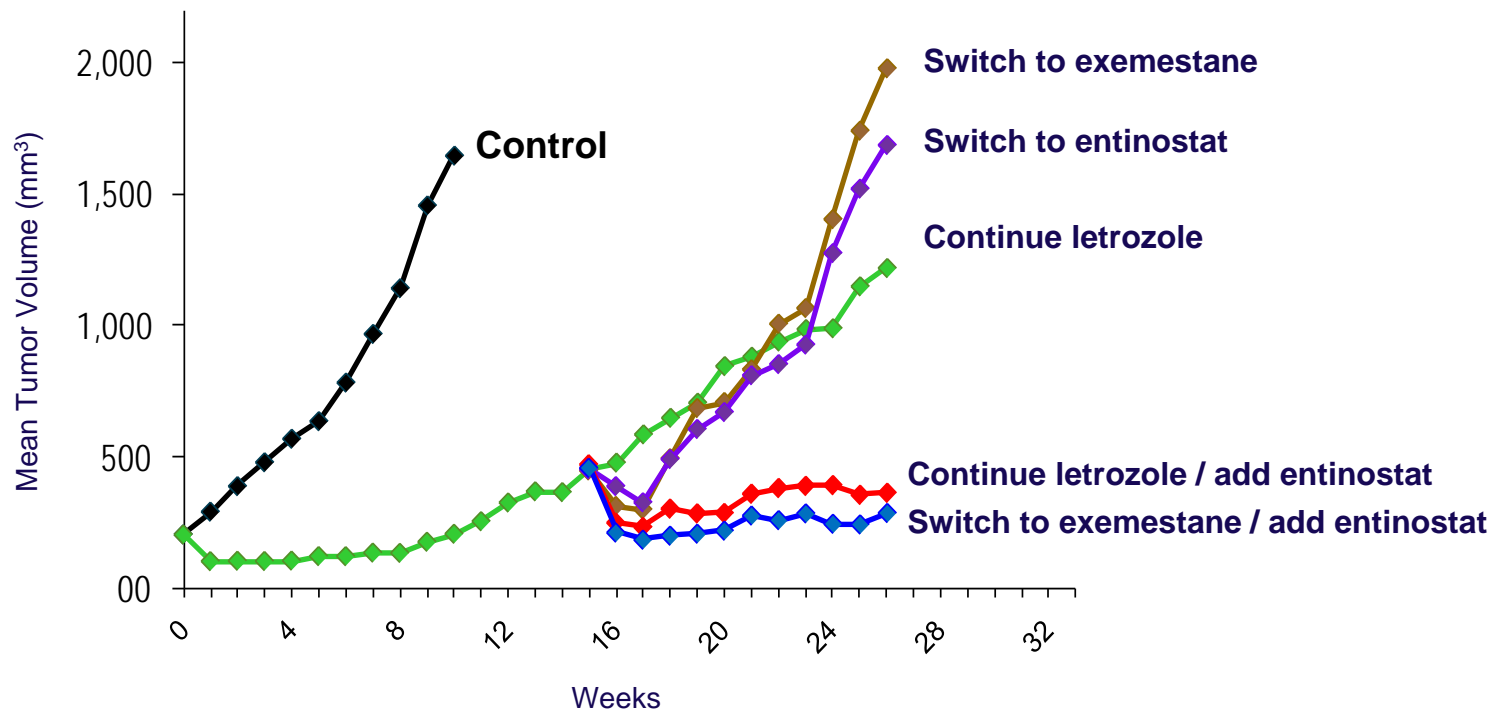
# Novel Science to Clinical Development

## The Story of Syndax

Briggs W. Morrison, MD

CEO, Syndax Pharmaceuticals  
Managing Director, MPM Capital

# Entinostat Overcomes Hormone Resistance



Sabnis GJ, Goloubeva OG, Kazi AA et al. Mol Cancer Ther Dec 2013

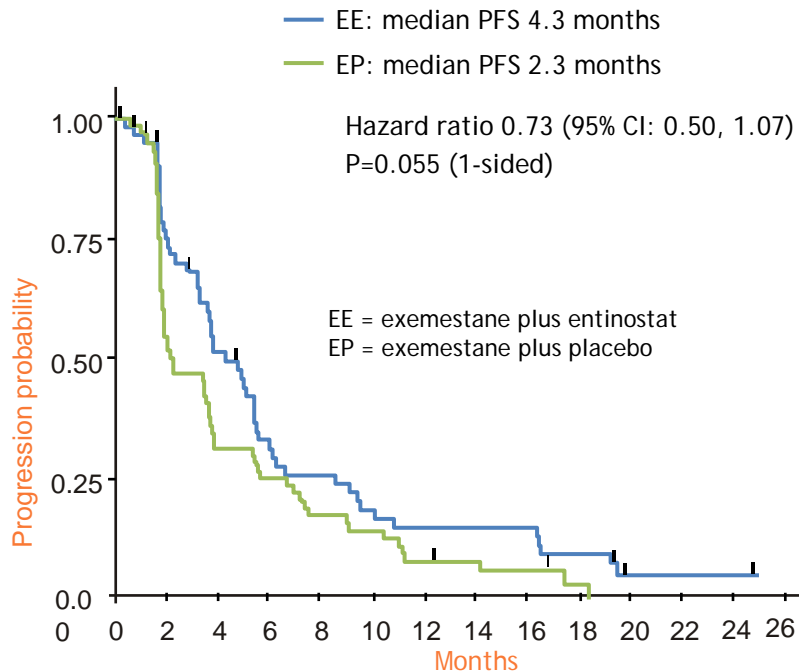
Cancer Progress by Defined Health  
New York, NY | March 8 - 9, 2016

DefinedHealth  
unconventional insight



# Entinostat Overcomes Hormone Resistance

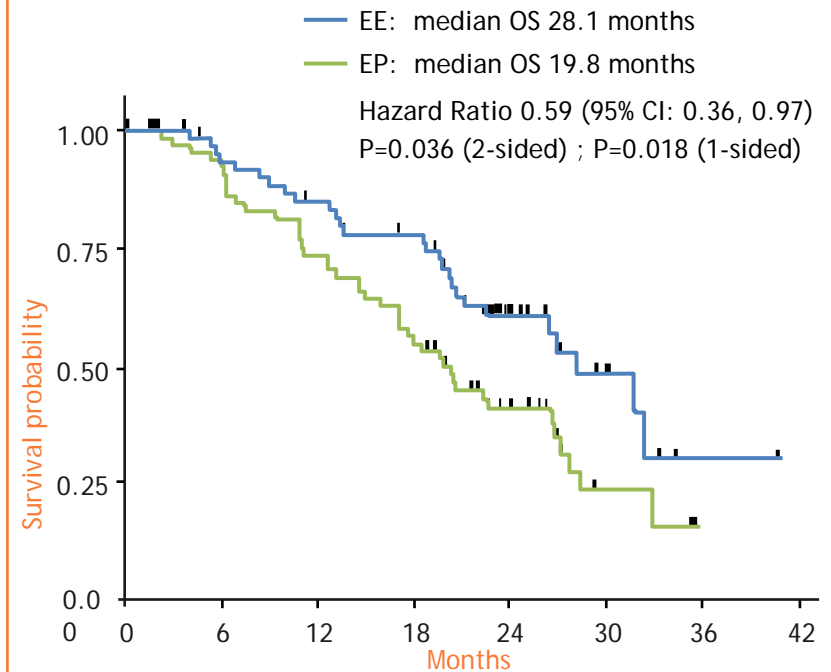
## Progression-Free Survival



|            |       |       |       |      |      |      |     |     |     |     |     |     |     |
|------------|-------|-------|-------|------|------|------|-----|-----|-----|-----|-----|-----|-----|
| Placebo    | 31/66 | 13/33 | 4/20  | 5/16 | 2/11 | 4/9  | 0/5 | 1/4 | 1/3 | 1/1 | 0/0 | 0/0 | 0/0 |
| Entinostat | 15/64 | 14/45 | 11/29 | 3/17 | 4/14 | 2/10 | 0/8 | 0/8 | 3/8 | 2/5 | 0/1 | 0/1 | 0/1 |

(#events / #at risk)

## Overall Survival



|            |      |       |       |      |      |     |     |
|------------|------|-------|-------|------|------|-----|-----|
| Placebo    | 4/66 | 13/60 | 12/47 | 8/35 | 5/18 | 1/3 | 0/0 |
| Entinostat | 4/64 | 5/55  | 4/49  | 9/43 | 3/21 | 2/9 | 0/1 |

(#events / #at risk)

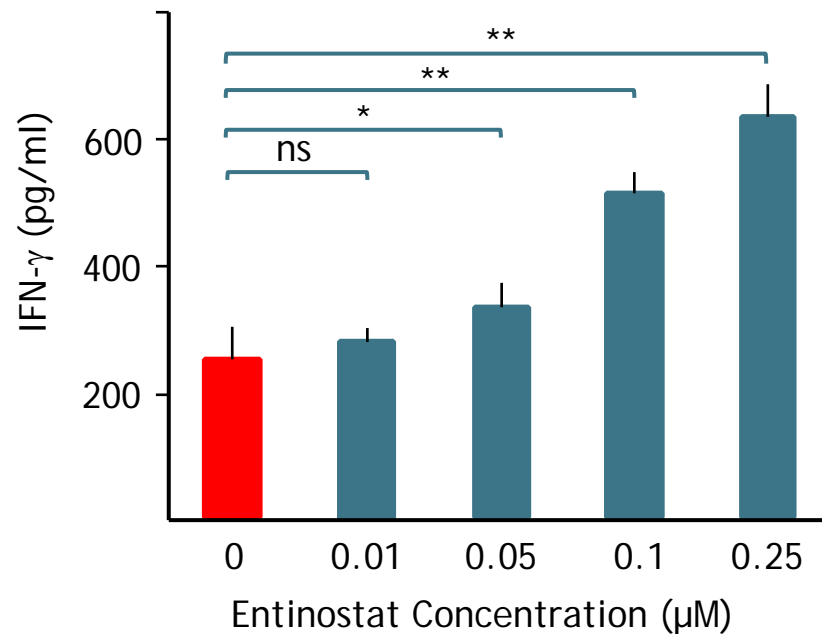
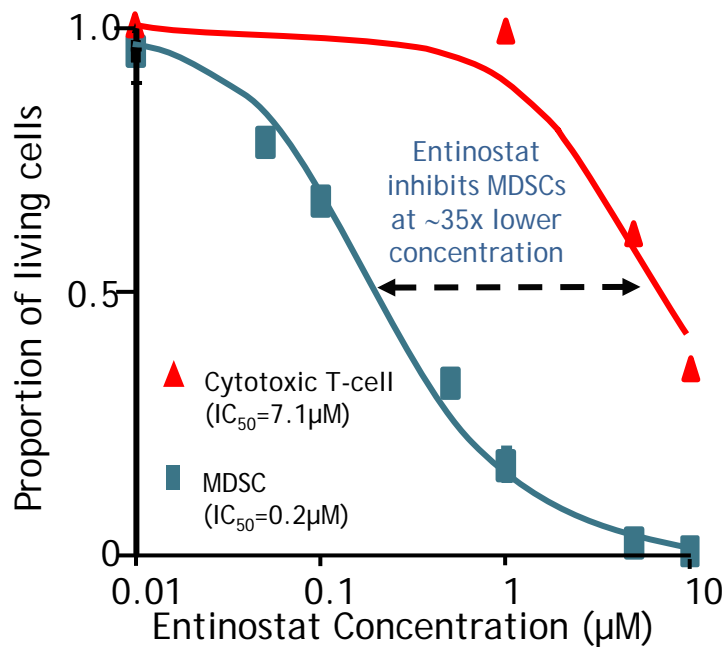
Yardley DA, Ismail-Khan RR, Melichar B et al. JCO 31:2128 2013

Cancer Progress by Defined Health  
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# Eradication of metastatic mouse cancers resistant to immune checkpoint blockade by suppression of myeloid-derived cells

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

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



\*  $P < 0.05$ , \*\*  $P < 0.01$ , ns, not significant

PNAS 111.32 (2014): 11774-11779

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THERAPEUTIC  
INSIGHT  
by Defined Health

CANCER  
PROGRESS  
by Defined Health

# Class I HDACis: MDSCs and T<sub>regs</sub>

- **Epigenetic silencing of retinoblastoma gene regulates pathologic differentiation of myeloid cells in cancer** – Youn et al. Nature Immunol 2013
- **Class I Histone Deacetylase Inhibitor Entinostat Suppresses Regulatory T Cells and Enhances Immunotherapies in Renal and Prostate Cancer Models** – Shen et al, PLoS One 2012
- **The regulatory T cell lineage factor Foxp3 regulates gene expression through several distinct mechanism mostly independent of direct DNA binding** – Xie et al PLoS Genetics 2015
- **Foxp3 regulatory T cell development and function require histone/protein deacetylase 3** – Wang et al Journ Clin Invest 2015

# Syndax sponsored clinical research

- Encore 601: Phase 1b/2 trial of entinostat + pembrolizumab in NSCLC and Melanoma
- Encore 602: Phase 1b/2 trial of entinostat+ atezolizumab in triple negative breast cancer
- Encore 603: Phase 1b/2 trial of entinostat + avelumab in ovarian cancer.

# Strategic Questions

- Further clinical development in hormone-receptor+ breast cancer vs. combination with immunotherapies?
- Further clinical development in entinostat versus novel molecules?