

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



1Q19 EARNINGS PRESENTATION | MAY 2019

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# 2019: Portfolio prioritization to drive value



## Entinostat - exemestane

Oral, Class I HDAC in HR+ mBC

- Potential positive OS data in 2019
- Efficacy post-CDK4,6 Tx
- Potential NDA filing in 2020
- Blockbuster potential

**Potential first combo to demonstrate survival benefit**

## SNDX-5613

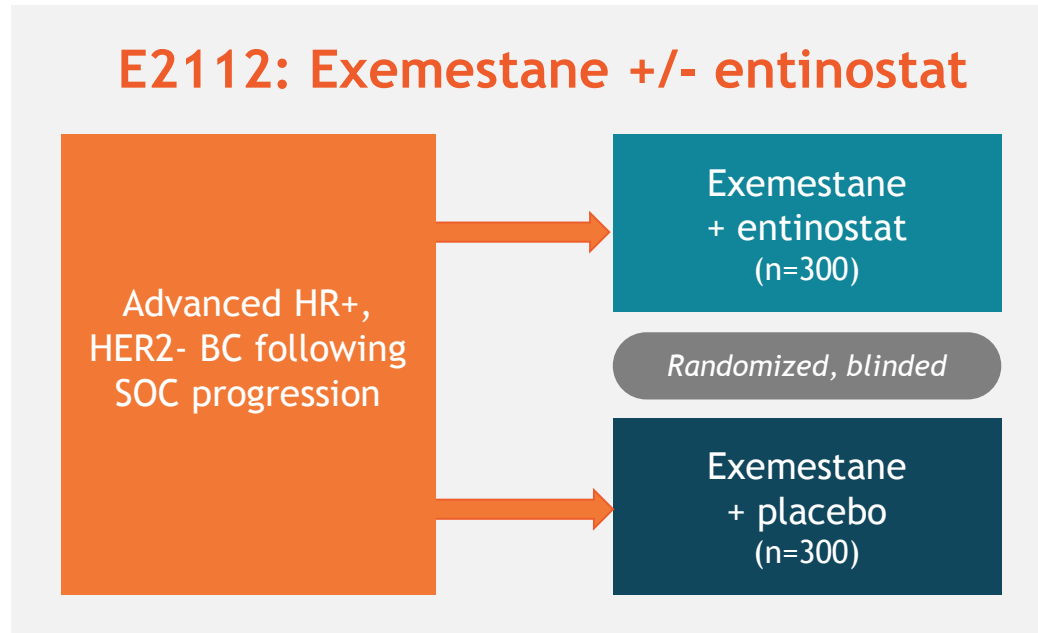
Oral, Menin inhibitor

- Blocks activity of MLL-fusion proteins
- IND filing est. 2Q, clinical data '19/'20
- Benefit expected in high need AML, ALL populations
- Blockbuster potential

**Targeted therapy provides fast to market opportunity**

HR+ mBC - hormone receptor positive metastatic breast cancer; MLL - mixed lineage leukemia; AML - acute myeloid leukemia; ALL - acute lymphoblastic leukemia

# Phase 3 E2112: Focused on overall survival



**Primary endpoint: OS**



## E2112 Trial Milestones

- ✓ **4Q18:** Accrual completed (n=608), PFS and interim OS analyses shared
- ✓ **2Q19:** Passed interim OS futility
  - **4Q19:** Next interim OS analysis
  - **2Q20:** Final OS analysis (if needed)

**Expect to file NDA ~6 months after positive OS data**

***A positive OS result allows filing for full regulatory approval***

# Blockbuster potential as 2<sup>nd</sup>/3<sup>rd</sup> line agent

## Leading treatment options - HR+, HER2- advanced breast cancer

### 1<sup>st</sup> line hormone Tx

Anastrozole or  
letrozole +/-  
CDK4,6 inhibitor

### 2<sup>nd</sup>/3<sup>rd</sup>/4<sup>th</sup> line hormone Tx

Anastrozole, Fulvestrant +/-  
CDK4,6 inhibitor or  
Afinitor-exemestane

**34,000 pts**

Entinostat-exemestane  
target population

### Chemo-Tx

Capecitabine, gemcitabine,  
eribulin

Source: DataMonitor 2017 Breast cancer: HR+/HER2- Disease Coverage Report; IQVIA Monthly treatment report (2018)

# SNDX-5613 targets novel fusion protein: Fusion proteins proven to be good candidates for targeted therapies

## Advantages

- Strong target validation
- Precise patient selection
- Big effect in small studies
- Molecular markers of disease status
- Rapid regulatory path

## Therapies targeting fusion proteins

### BCR-ABL



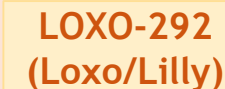
### EML4-ALK



### NTRK Fusions

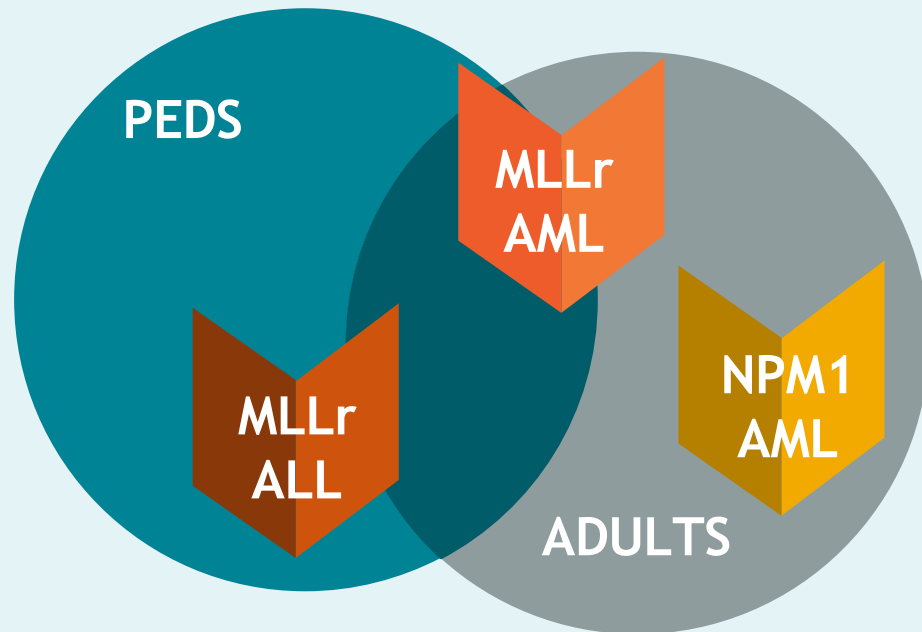


### RET Fusions



# SNDX-5613: potential best-in-class, targeted, oral agent with single agent activity and fast to market potential

Phase 1/2 trial population:  
MLLr adult, MLLr peds, NPM1 mut AML

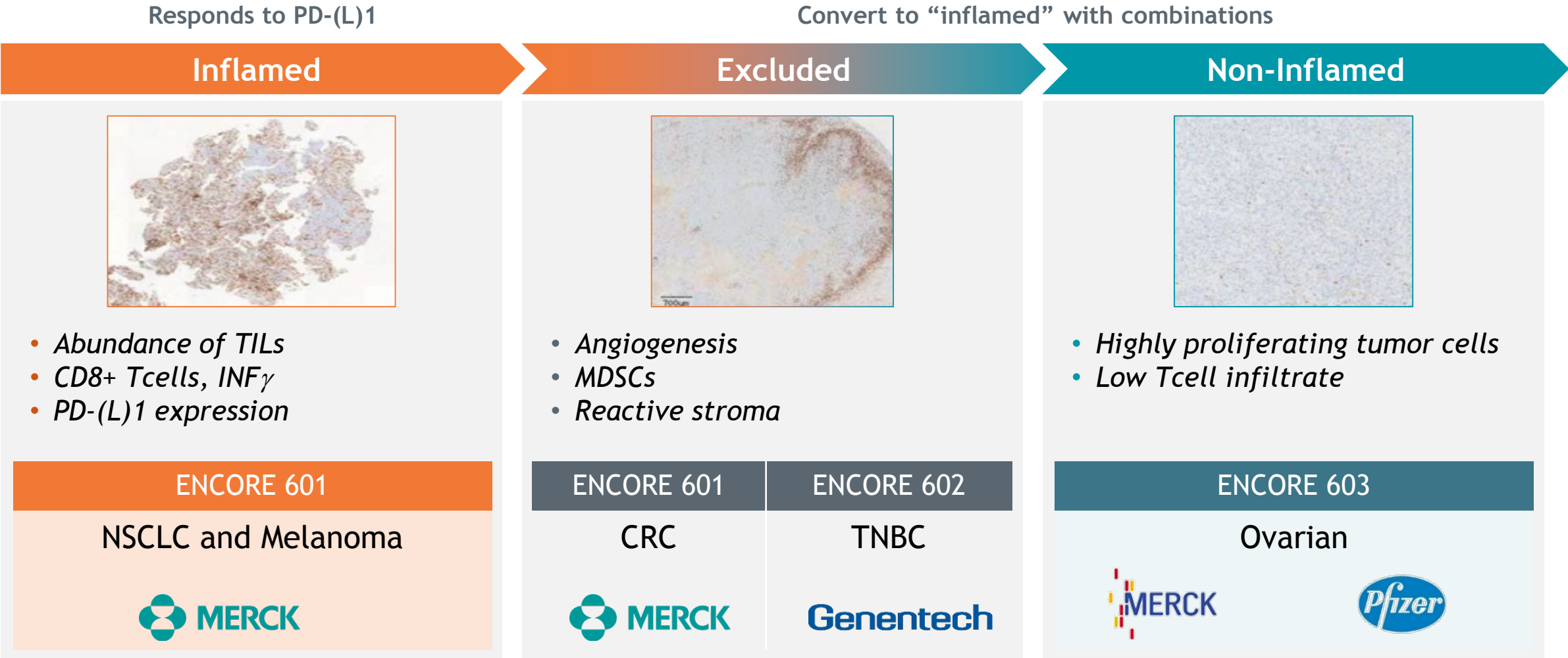


## Defined fast to market pathway

- IND filing est. 2Q19; Phase 1 to follow
  - Early efficacy possible as early as year-end 2019
- MLLr and NPM1 identified today with standard screening protocols
- No approved therapies targeting MLLr or NPM1 acute leukemias
  - \$\$B commercial opportunity



# Entinostat ENCORE program tested PD-(L)1 combos across immune phenotypes



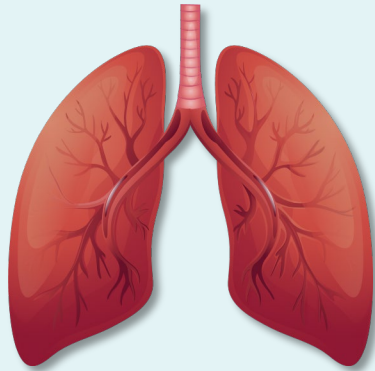
Source: Hedge, et al. *Clin Cancer Res*; 22.8 (2016): 1865-1874.



# ENT-Keytruda shown to reverse resistance to anti-PD-1 Tx in NSCLC and MEL

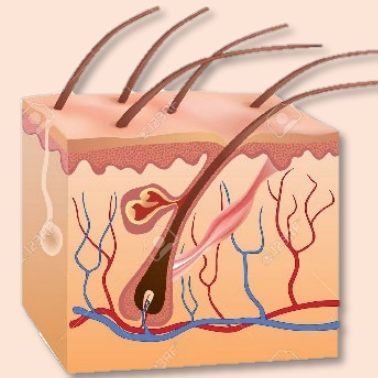
Trial cohorts enrolled patients whose disease had progressed on/after anti-PD-1 therapy

## Biomarker selected NSCLC



*ENT shown to down regulate myc activity;  
re-sensitizing pts to PD1 w/8 months mDoR*

## Melanoma



*19% ORR, 36% CBR\*; 13mo mDOR, 4.2mo mPFS  
similar results in pts who had prior CTLA4*

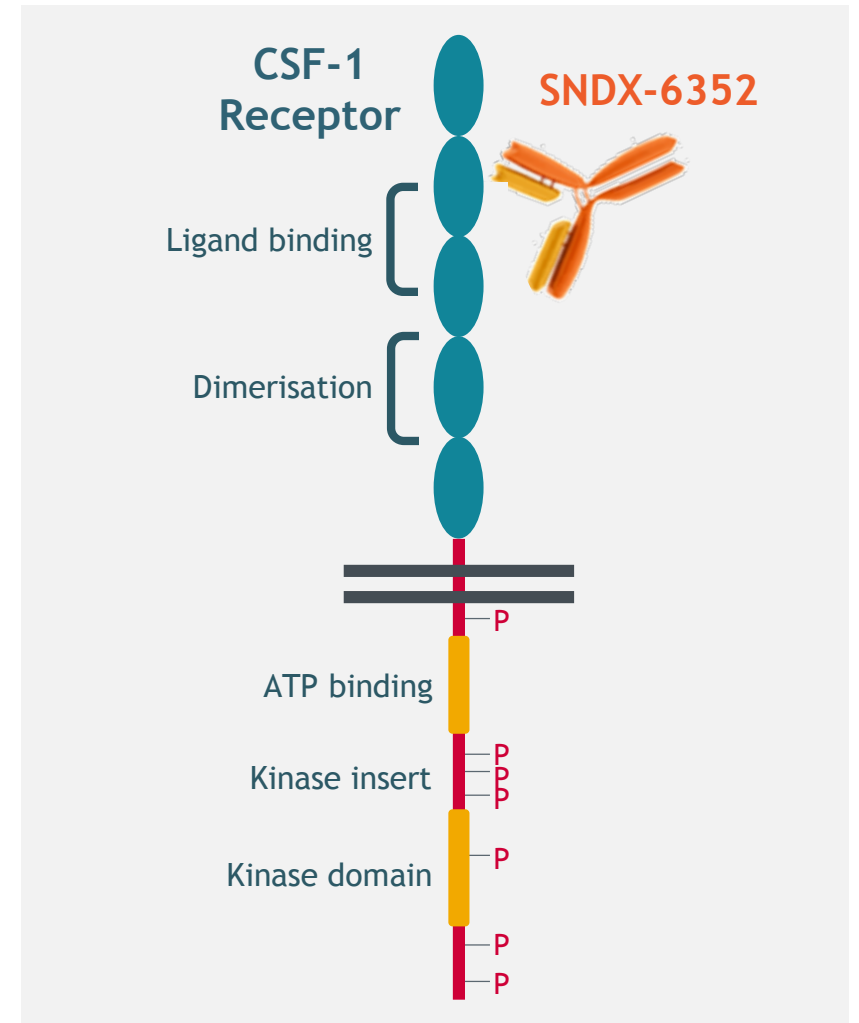
*“The overall medical benefit is impressive, the study is very positive for seeing the potential role for epigenetic therapy in the setting of immunotherapy.” - Dr. S. Baylin  
(AACR 2019 oral presentation discussant)*

CBR - Clinical Benefit Rate includes patients with CR, PR or SD >6 months; Source: Ramalingam, S, et al; AACR Annual meeting 2019; Sullivan, R, et al; AACR Annual meeting 2019

# SNDX-6352: Pursuing a novel indication

High affinity, IgG4 ( $K_D = 4-8$  pM)

- ✓ Chronic graft versus host disease (cGVHD)
  - Study initiated in 4Q18
- ✓ Multiple ascending dose (MAD, solid tumors) ongoing
  - RP2D expected in 2Q19
- ✓ Combination study with IMFINZI (durvalumab, AZ) ongoing
  - RP2D expected in 2Q19



CSF-1R - colony stimulating factor-1 receptor; RP2D - recommended Phase 2 dose.  
Source: Ordentlich, P. et al SITC 2016.

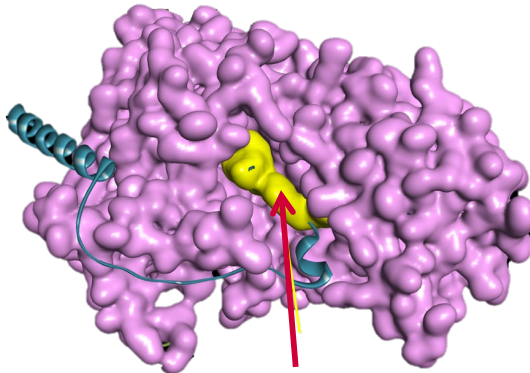
# Proven ability to build the pipeline

3Q16: UCB



SNDX-6352

4Q17: Allergan/Vitae



Menin-MLLr  
inhibitors

- Established relationships enhance identification and access to quality assets
- Clinical development leadership enables competitive advantage
- Business development continues to be a core strength of our business

## March 2019 financing: \$27.4 million net proceeds extends cash runway



- Completed deal with key investors, led by BVF
- Issued 4.6M shares and prefunded warrants @ \$6.00 (premium to market) and 4.6 M series warrants priced at \$12 and \$18
  - Warrants expire on the earlier of E2112 positive OS data + 3 months or Dec 31, 2020
- 31.6 million total shares outstanding post financing

# Q1 2019 financial highlights and 2Q, full-year 2019 guidance

Ticker		SNDX (NASDAQ)
As of March 31, 2019		
Cash and short-term investments		\$92.7 million
Shares Outstanding*		31.6 million
2019 2Q and full year Operating Expense Guidance		
	2Q 2019	2019
Research and Development	\$9 - 10 M	\$46 - 50 M
Total Operating Expenses^	\$13 - 14 M	\$60 - 64 M

\* Includes 27.1 million common shares and pre-funded warrants to purchase 4.5 million common shares

^ Includes \$1.5 and \$6 million non-cash stock compensation expense for 2Q 2019 and for 2019, respectively

# Upcoming milestones

ENTINOSTAT (Class 1 specific HDAC inhibitor)	2Q19	3Q19	4Q19	1H20
E2112 - upcoming OS analyses*			●	●

\* Final 1H20 OS analysis will only be conducted if needed

SNDX-5613 (Menin inhibitor)	2Q19	3Q19	4Q19	1H20
Investigational New Drug (IND) application	●			
Potential for early efficacy in relapsed refractory AML			▬	

SNDX-6352 (anti-CSF-1R mAB)	2Q19	3Q19	4Q19	1H20
Identify recommended Phase 2 dose and schedule	●			
Preliminary efficacy in chronic GVHD		●		



Thank you. Questions?

Syndax 