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

Syndax

2Q20 EARNINGS PRESENTATION

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Syndax pipeline addresses key areas of unmet need in cancer

SNDX-5613
Menin Inhibitor
Leukemias

- Acute leukemias
- Initial Ph 1 data provides clinical evidence of efficacy
- RP2D expected YE20
- Ph 1 data early 2021

Axatilimab
anti-CSF1R mAB
Chronic GVHD

- Macrophage driven diseases
- Clinical POC for chronic GVHD achieved
- Ph 1 data expected 4Q20

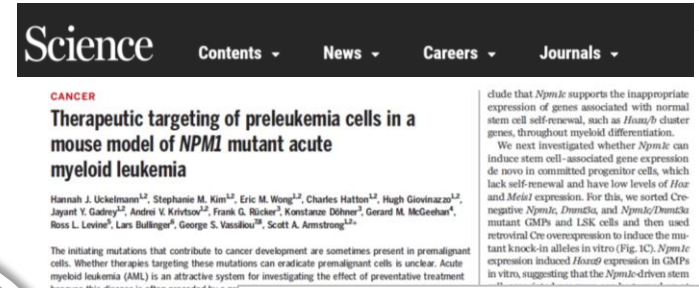
Entinostat
Class I
HDAC Inhibitor

- Ph 3, E2112, in HR+/HER2- mBC did not meet primary endpoint of OS
- Program has been deprioritized

SNDX-5613: Breakthrough targeted therapy for acute leukemia

Advantages

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



Science Contents News Careers Journals

CANCER

Therapeutic targeting of preleukemia cells in a mouse model of *NPM1* mutant acute myeloid leukemia

Hannah J. Uckelmann[1,2], Stephanie M. Kim[1,2], Eric M. Wong[1,2], Charles Hatton[1,2], Hugh Giovinazzo[1,2], Jayant Y. Gadrey[1,2], Andrei V. Krivtsov[1,2], Frank G. Rücker[3], Konstanze Döhner[3], Gerard M. McGeehan[4], Ross L. Levine[5], Lars Bullinger[6], George S. Vassiliou[7,8], Scott A. Armstrong[1,2]*

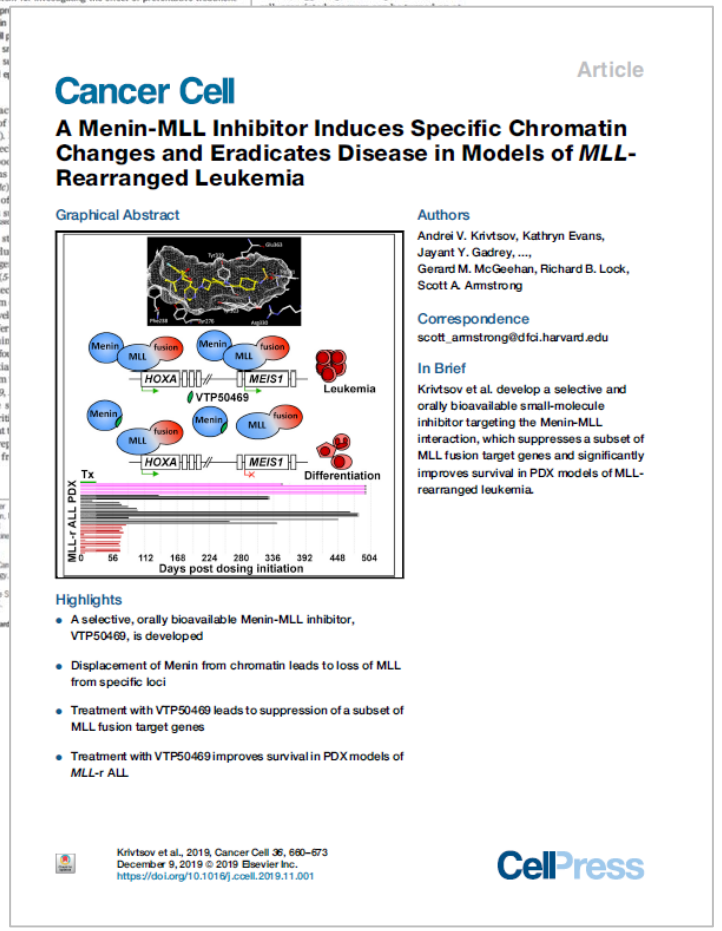
The initiating mutations that contribute to cancer development are sometimes present in premalignant cells. Whether therapies targeting these mutations can eradicate premalignant cells is unclear. Acute myeloid leukemia (AML) is an attractive system for investigating the effect of preventative treatment because this disease is often preceded by a pr… syndrome). In *Npm1c/Dnmt3a* mutant knock-in … by a period of extended myeloid progenitor cell … be reversed by oral administration of a s… matin complex. These preclinical results s… oping AML might benefit from targeted e…

…leophosmin (*NPM1*) mutant ac… loid leukemia (AML) is one of … common types of AML (*1*–*3*). … its high prevalence, the mec… of leukemogenesis is still poo… and targeted therapy options … *NPM1* gene mutations (*NPM1c*) …asmic localization of NPM1 and of… …ith other mutations in genes s… *…ethyltransferase 3A* (*DNMT3A*[Ross]) … …ukemias express a distinctive s… gene expression pattern that inclu… …box cluster A and B (*HOXA/B*) ge… …eir DNA-binding cofactor MEIS1 (*5*… …mans, *DNMT3A* mutations are detec… …he most primitive hematopoietic stem … compartment, often long before the devel… ment of leukemia, a condition often refer… to as clonal hematopoiesis of indetermin… potential (CHIP) (*9*). *NPM1* mutations are fo… in committed progenitors and differentia… myeloid cells in AML but are absent from … stem cell and lymphoid compartments (*9*, … is suggests that *NPM1c* may induce s… …wal in myeloid progenitors as a crit… …n the development of AML and that t… …t progenitor self-renewal may reg… …itical step in the progression fr… …AML.

…Pediatric Oncology, Dana-Farber Cancer … …vision of Hematology/Oncology, Boston, … …Children's Hospital and Harvard Medical … …MA, USA. [7]Department of Internal Medicine … …ital of Ulm, Ulm, Germany. [8]Syndax … …s, Inc., Waltham, MA, USA. [9]Center for … …leukemias, Memorial Sloan Kettering Can… …ork, NY, USA. [10]Department of Hematology … …l Tumor Immunology, Charité University … …erlin, Germany. [11]Wellcome-MRC Cambridge S… …e, University of Cambridge, Cambridge, UK. … …e Trust Sanger Institute, Cambridge, UK. …onding author. Email: scott_armstrong@dfci.harvard…

clude that *Npm1c* supports the inappropriate expression of genes associated with normal stem cell self-renewal, such as *Hoxa/b* cluster genes, throughout myeloid differentiation.

We next investigated whether *Npm1c* can induce stem cell–associated gene expression de novo in committed progenitor cells, which lack self-renewal and have low levels of *Hoxa* and *Meis1* expression. For this, we sorted Cre-negative *Npm1c*, *Dnmt3a*, and *Npm1c/Dnmt3a* mutant GMPs and LSK cells and then used retroviral Cre overexpression to induce the mutant knock-in alleles in vitro (Fig. 1C). *Npm1c* expression induced *Hoxa9* expression in GMPs in vitro, suggesting that the *Npm1c*-driven stem



Article

Cancer Cell

A Menin-MLL Inhibitor Induces Specific Chromatin Changes and Eradicates Disease in Models of *MLL*-Rearranged Leukemia

Graphical Abstract

Authors
Andrei V. Krivtsov, Kathryn Evans, Jayant Y. Gadrey, ..., Gerard M. McGeehan, Richard B. Lock, Scott A. Armstrong

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In Brief
Krivtsov et al. develop a selective and orally bioavailable small-molecule inhibitor targeting the Menin-MLL interaction, which suppresses a subset of MLL fusion target genes and significantly improves survival in PDX models of MLL-rearranged leukemia.

Highlights

- A selective, orally bioavailable Menin-MLL inhibitor, VTP50469, is developed
- Displacement of Menin from chromatin leads to loss of MLL from specific loci
- Treatment with VTP50469 leads to suppression of a subset of MLL fusion target genes
- Treatment with VTP50469 improves survival in PDX models of *MLL*-r ALL

Krivtsov et al., 2019, Cancer Cell 36, 660–673
December 9, 2019 © 2019 Elsevier Inc.
https://doi.org/10.1016/j.ccell.2019.11.001

CellPress

Projecting pre-clinical PK/PD to target clinical exposure

Target PK Profile Requirements

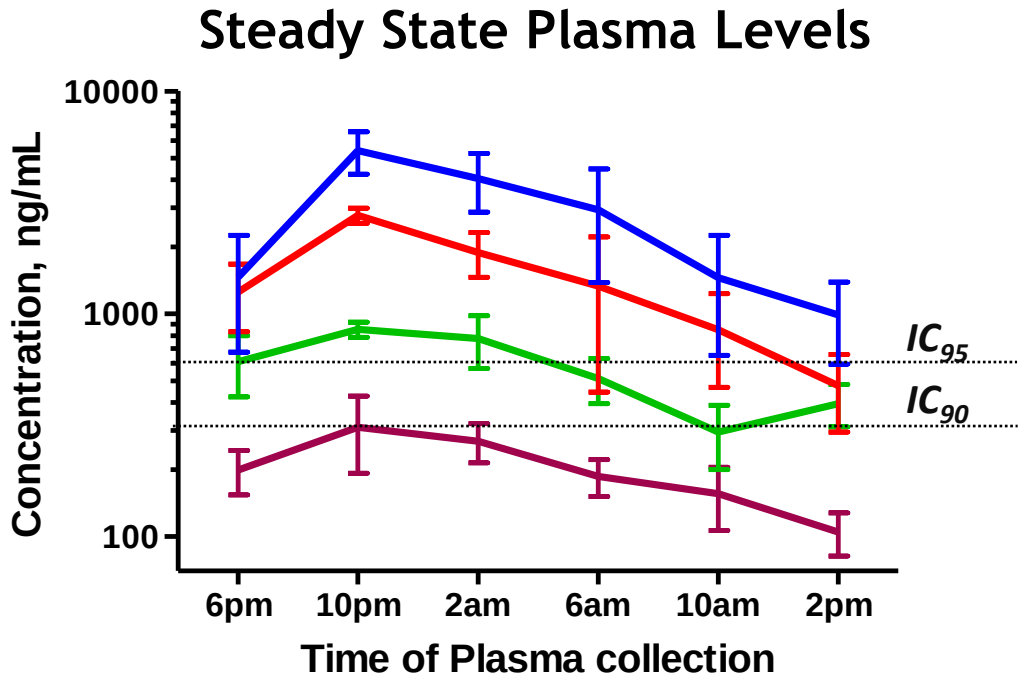
Maintain steady state levels above IC_{95} (~600 ng/mL) for most of dosing interval

AND

Maintain C_{min} level above projected IC_{90} (~300 ng/mL)

AND

Minimum 24 h AUC of ~30,000 ng*h/mL

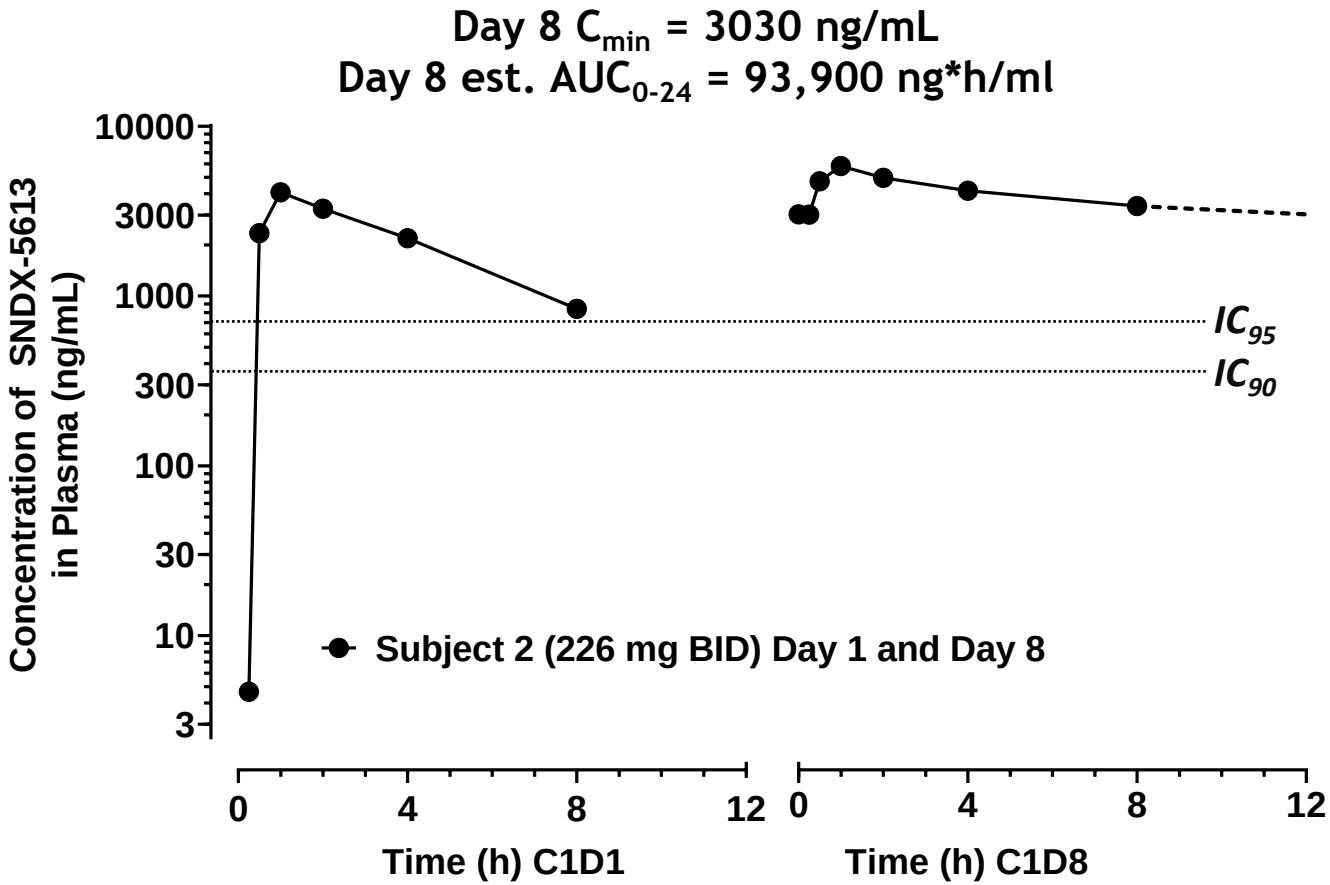


DOSE STRENGTH %	AVE CONC ng/ml	AUC_{0-24} ng*hr/ml
0.025	203	4900
0.05	573	13700
0.10	1425	34200
0.20	2713	65100

Patient #2: 226 mg PO q12h

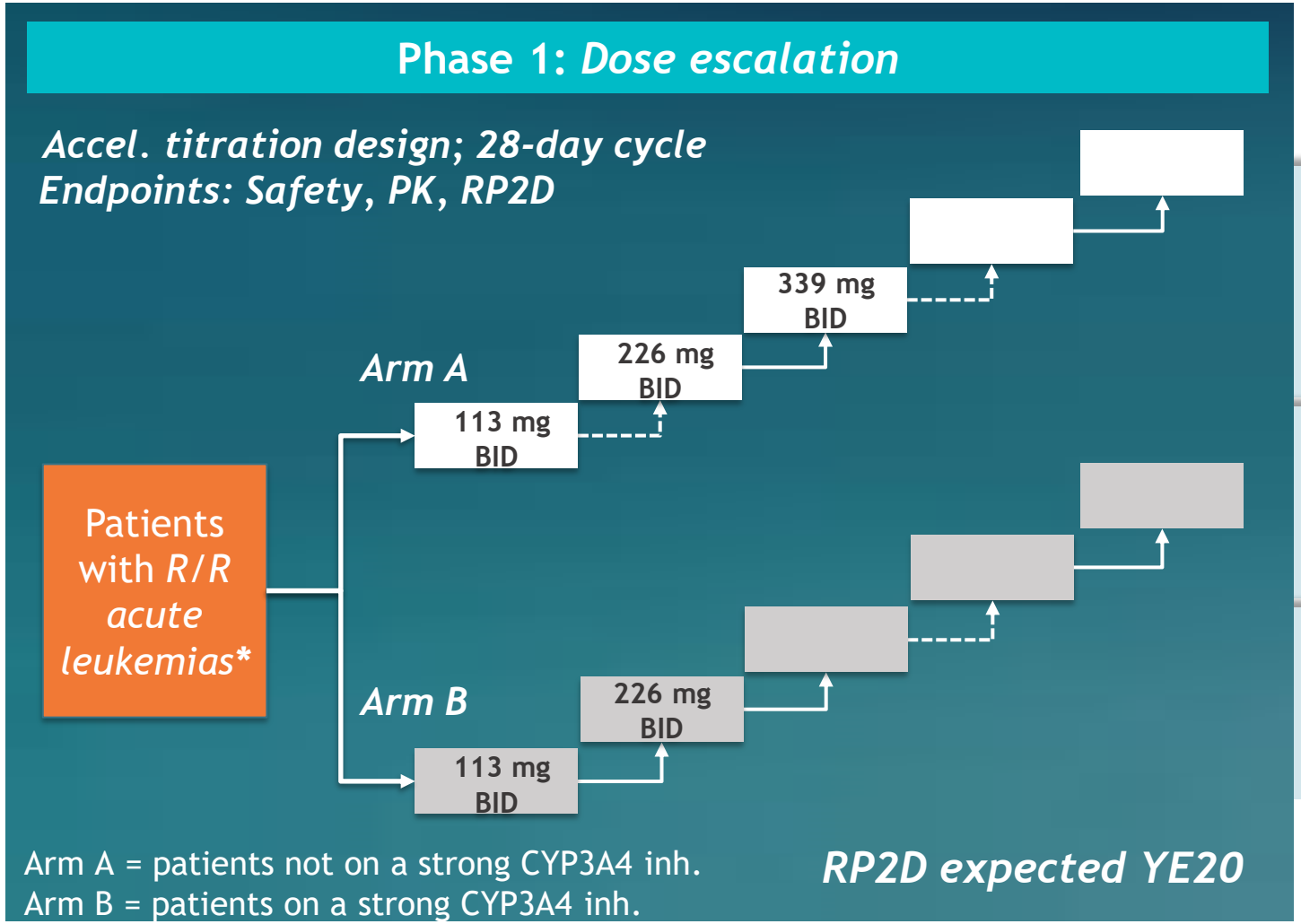
Patient Characteristics

Gender, Age	Female, 69 yr old
Diagnosis	Refractory MPAL
Mutational status	MLL-TET1 fusion FLT3 ITD
Prior lines of therapy	2 (chemo, gilteritinib)
SNDX-5613 dose	226 mg PO q12 h
DLT period	No DLTs; Grade 2 QTc → resolved with dose reduced to 113 mg q12h
Day 28 response	CRi; beyond DLT period has improved to CR while on reduced dose



CR = Complete response, CRh = Complete response with partial hematologic recovery, CRi = Complete response with incomplete hematologic recovery

Strong, widespread support to accelerate '5613 development



FDA agrees to multiple AUGMENT-101 enhancements

1. Focusing trial to enroll only MLL-r or NPM1 acute leukemia
2. Allowing expansion of cohorts showing efficacy
3. Inclusion of pediatric patients (>30 days old)

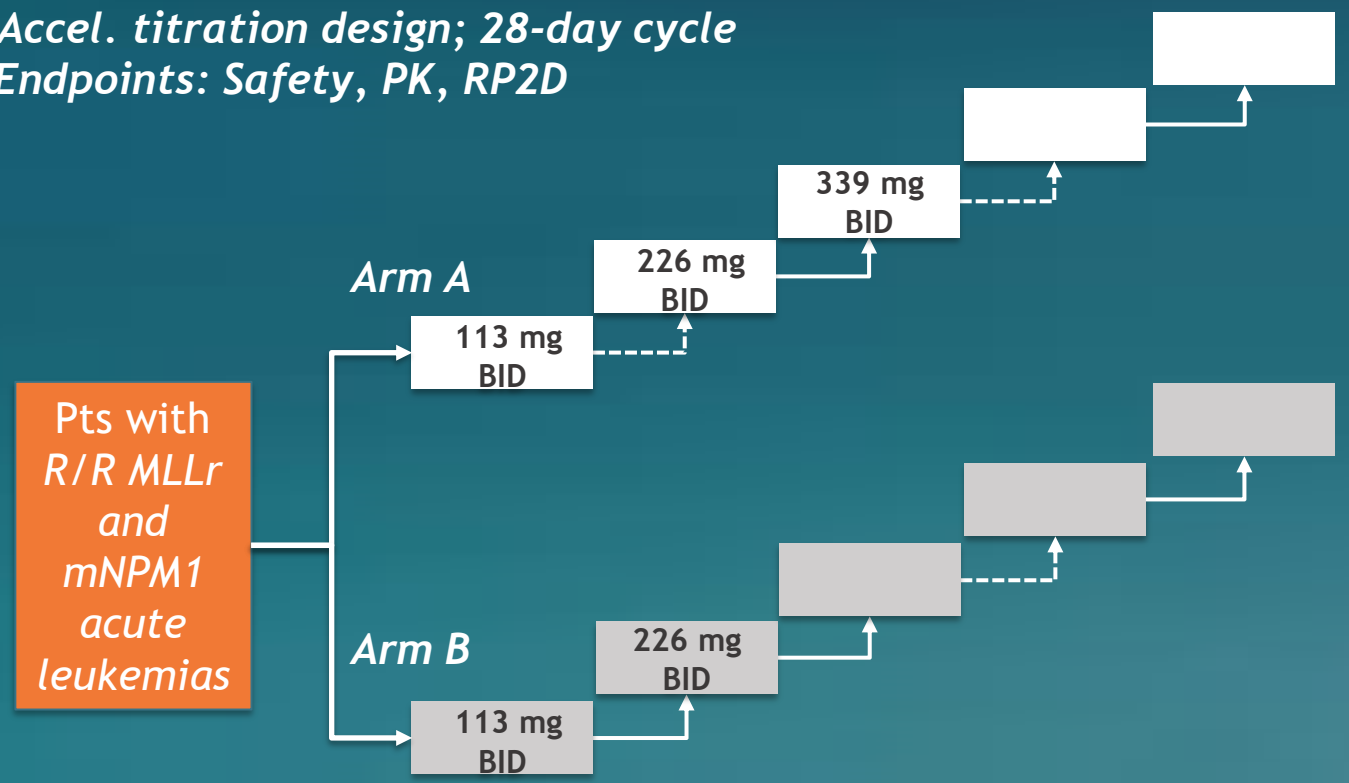
Ph 1 data early 2021

* Unselected population; ^ CR = Complete response, CRh = Complete response with partial hematologic recovery; MLL-r – mixed lineage leukemia rearranged; NPM = nucleophosmin

AUGMENT-101: Phase 1/2 trial of SNDX-5613, in patients with acute leukemia

Phase 1: *Dose escalation*

Accel. titration design; 28-day cycle
Endpoints: Safety, PK, RP2D



Arm A = patients not on a strong CYP3A4 inh.
Arm B = patients on a strong CYP3A4 inh.

Phase 2: *Expansion*

Pursuing rapid regulatory path

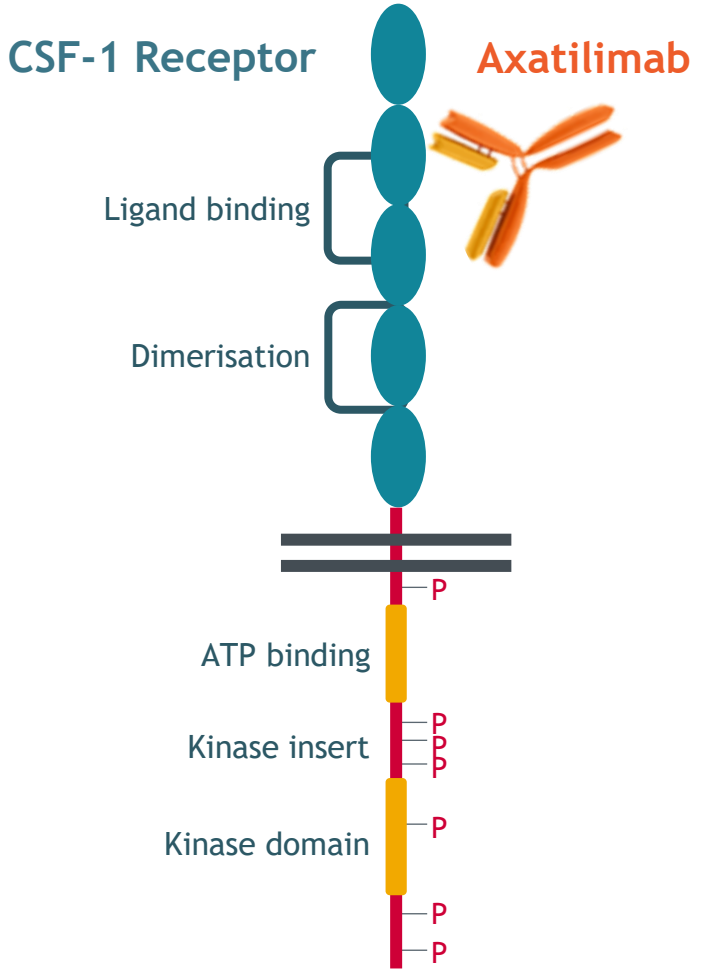
- MLL-r ALL
- MLL-r AML
- NPM1 mut AML

Primary endpoint:
CR Rate (CR + CRh^)

^ CR = Complete response, CRh = Complete response with partial hematologic recovery; MLL-r – mixed lineage leukemia rearranged; NPM = nucleophosmin

Axatilimab: CSF-1R mAB with potential best-in-class profile

- Axatilimab Phase 1 MAD data presented at AACR Virtual Meeting I
  - Rapid and sustained depletion of circulating pro-inflammatory monocytes observed at all doses
  - Demonstrated tolerability and robust PD biomarker modulation



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

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

Axatilimab: Significant potential in cGVHD

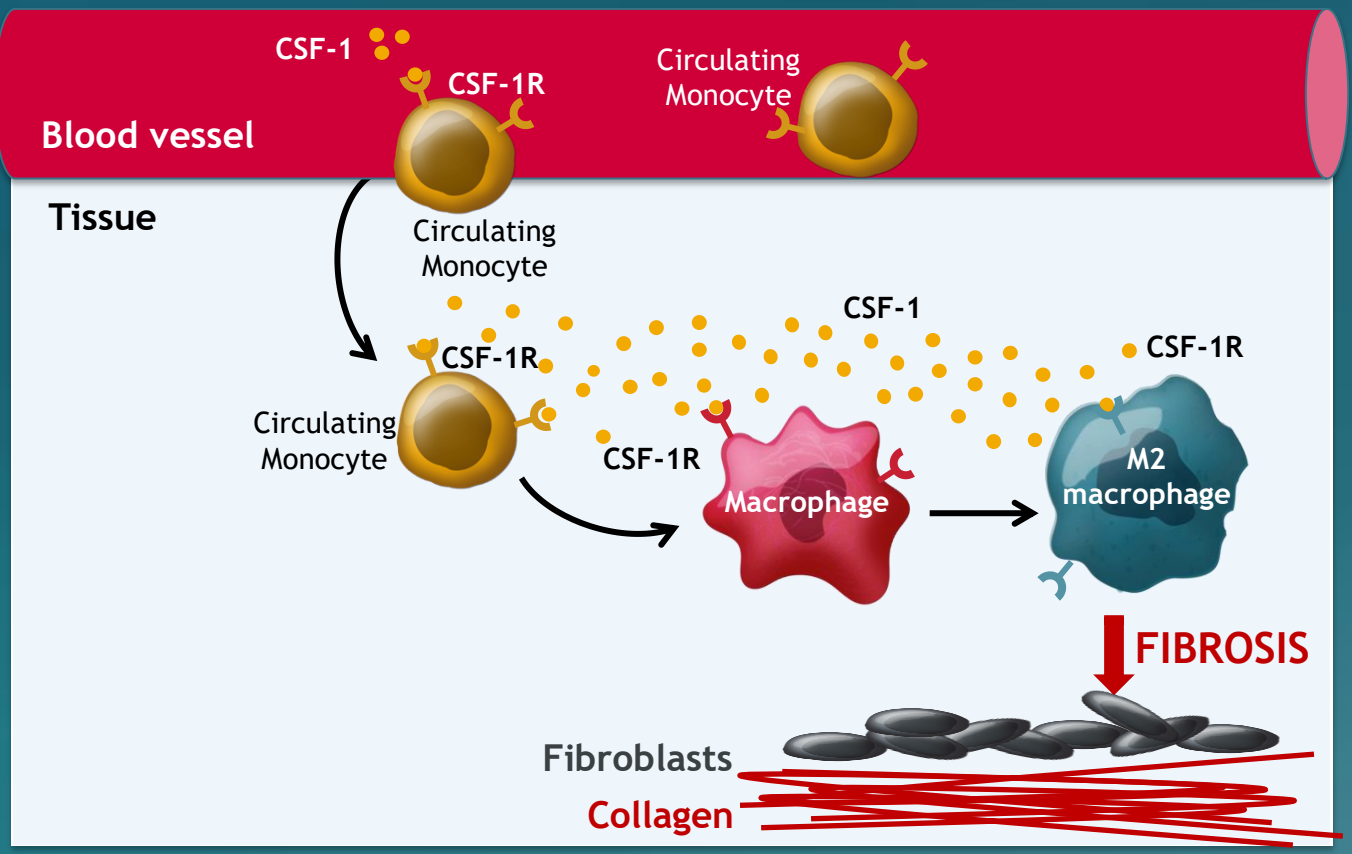
cGVHD develops in 40% of HSCT[1,2]

- **US prevalence ~14,000[2]**

Pre-clinical evidence suggest CSF-1-dependant macrophages mediate cGVHD[3]

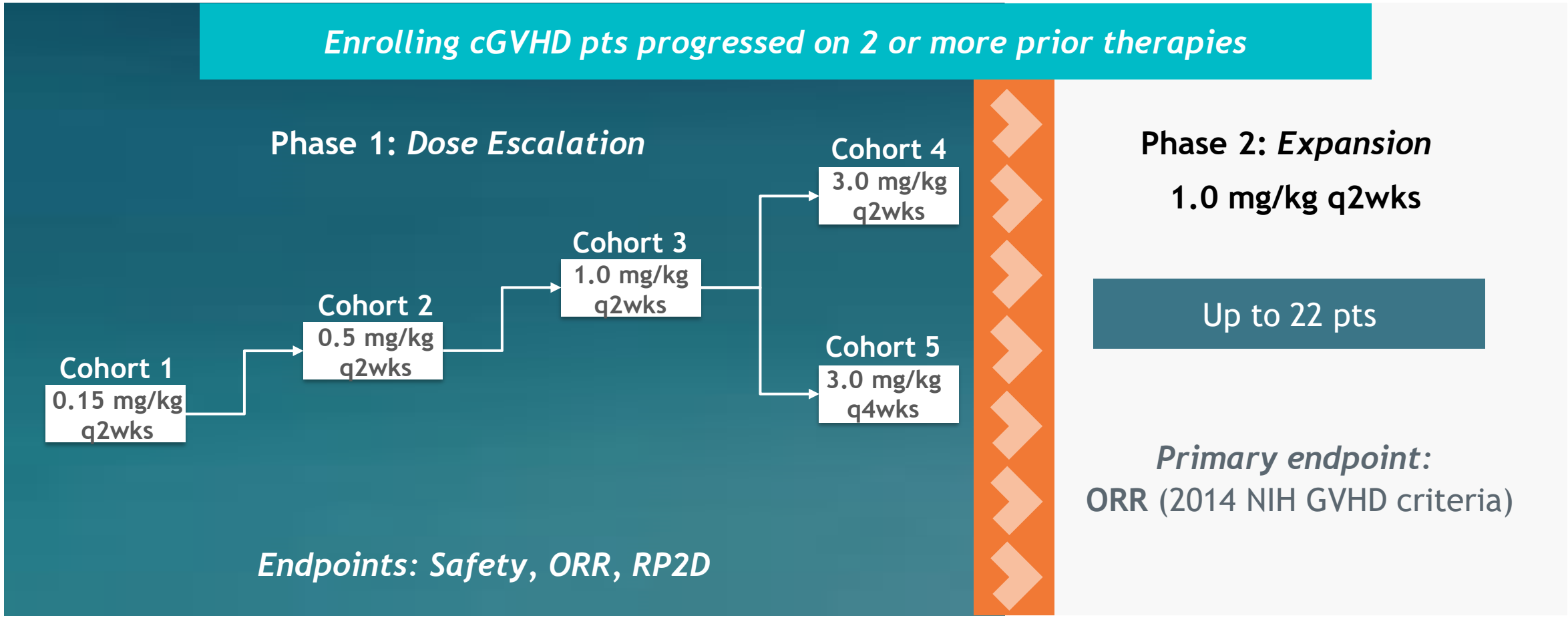
Ph 1/2 trial enrolling; Ph 1 data 4Q20

Signaling through CSF-1R may play a meaningful role in the management of chronic GVHD



Source: 1. SmartAnalyst 2017 SmartImmunology Insights chronic GVHD report.; 2. Bachier, CR. et al. ASH annual meeting 2019; abstract #2109 Epidemiology and Real-World Treatment of cGVHD Post Allogeneic HSCT: A U.S. Claims Analysis.; 3.Alexander, KA et al., J Clin Invest. 2014;124(10):4266-4280. Figure Adopted from MacDonald, K.P.A. et al., BLOOD, 5 (129) 13-21; HSCT - Hematopoietic stem cell transplantation

Axatilimab: Phase 1 established early proof of concept in cGVHD, Phase 2 designed to identify optimal dose



Anticipate sharing complete Phase 1 data at medical meeting in 4Q20

Proven ability to build the pipeline

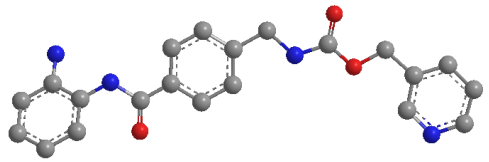
Business development continues to be a core strength of our business

Clinical development leadership enables competitive advantage

Established relationships enhance identification and access to quality assets

From Bayer

Entinostat

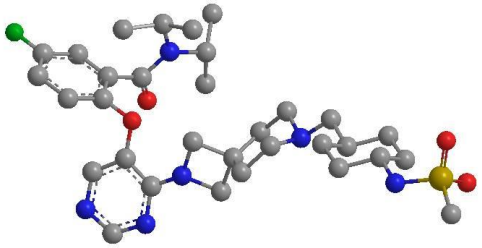


From UCB

Axatilimab

From Allergan/Vitae

Menin-MLL inhibitors



Financial highlights and 2H20 financial guidance

2Q 2020: Equity offering at $18.00, net proceeds of $107.9 M

Ticker	SNDX (NASDAQ)	
Cash and short-term investments (at Jun 30, 2020)	$186.8 million	
Shares Outstanding* (at Aug 3, 2020)	44.1 million	
3Q and 2020 Operating Expense Guidance		
	3Q 2020	**2H20**
Research and Development	$14-16 M	$30-35 M
Total Operating Expenses^	$19-21 M	$40-45 M

* *Includes 38.5 million common shares and pre-funded warrants to purchase 5.6 million common shares;*
^ *Includes $2.0 million non-cash stock compensation expense per quarter*

Thank you. Questions?

Syndax