

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



3Q20 EARNINGS PRESENTATION

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Syndax pipeline targets indications with significant unmet need

SNDX-5613 Menin Inhibitor

- Acute leukemias
- Ph 1 data validates new leukemia target
- Ph 2 initiation expected early 2021
- Fast-to-market regulatory path

Axatilimab Anti-CSF-1R mAB

- Macrophage driven diseases
- POC for cGVHD
- Initiation of pivotal trial expected by YE20
- Inflammatory/fibrotic franchise opportunity

Development opportunities

- Focused on expanding pipeline through new asset acquisition

SNDX-5613: Breakthrough targeted therapy for acute leukemia

Advantages

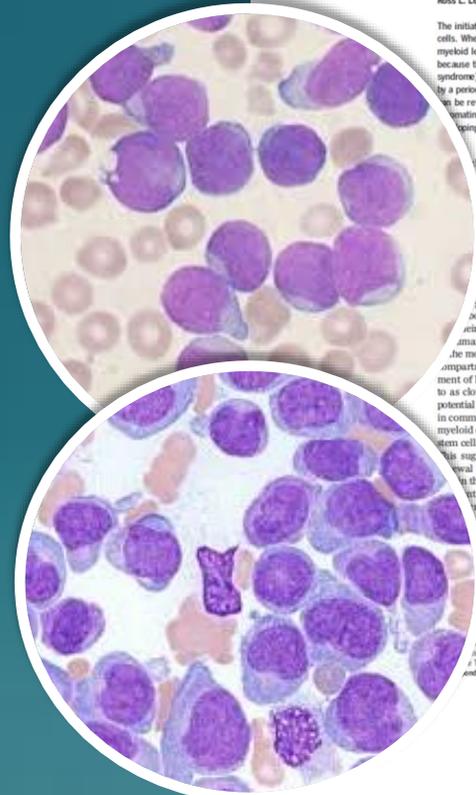
Strong target validation

Precise patient selection

Big effect in small studies

Molecular markers of disease status

Potential for rapid regulatory path



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. Wang^{1,2}, Charles Hatten^{1,2}, Hugh Glavinatzis^{1,2}, Jayant Y. Gadrey^{1,2}, Andrei V. Krivtsov^{1,2}, Frank G. Rücker¹, Konstanze Döhner¹, Gerard M. McGeehan¹, Ross L. Levine¹, Lars Bullinger¹, George S. Vassiliou^{1,3}, Scott A. Armstrong^{1,2,4}

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 preleukemic syndrome. In *Npm1c/Dnmt3a* mutant knock-in mice, we found that a period of extended myeloid progenitor cell self-renewal can be reversed by oral administration of a small molecule inhibitor of the *Npm1* complex. These preclinical results suggest that targeting AML might benefit from targeted eradicating of preleukemic cells.

Acute myeloid leukemia (AML) is one of the most common types of AML (1-3). Due to its high prevalence, the mechanisms of leukemogenesis are still poorly understood, and targeted therapy options are limited. *NPM1* gene mutations (*NPM1c*) cause aberrant localization of NPM1 and of other mutations in genes at *retrovirus* sites (*DNMT3A*)^{4,5}. *NPM1c* leukemias express a distinctive set of gene expression patterns that include *HOXA* cluster A and B (*HOXA/B*) genes. The DNA-binding cofactor MEIS1 (*MEIS1*) is a transcription factor that binds to *HOXA/B* sites. *DNMT3A* mutations are detected in the most primitive hematopoietic stem cell compartment, often long before the development of leukemia, a condition often referred to as clonal hematopoiesis of indeterminate potential (CHIP) (6). *NPM1* mutations are found in committed progenitors and differentiated myeloid cells in AML, but are absent from stem cell and lymphoid compartments (6, 7). This suggests that *NPM1c* may induce self-renewal in myeloid progenitors as a critical step in the development of AML, and that targeting progenitor self-renewal may represent a critical step in the progression of AML.

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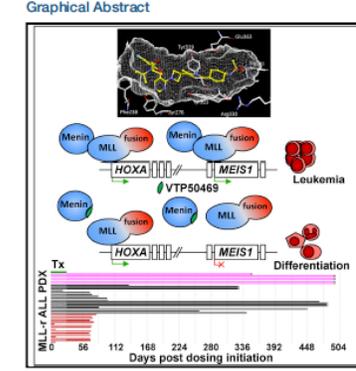
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clude that *Npm1c* supports the inappropriate expression of genes associated with normal stem cell self-renewal, such as *Hoxa/B* cluster genes, throughout myeloid differentiation. We next investigated whether *Npm1c* can induce stem cell-associated 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 *Hoxa* expression in GMPs in vitro, suggesting that the *Npm1c*-driven stem

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



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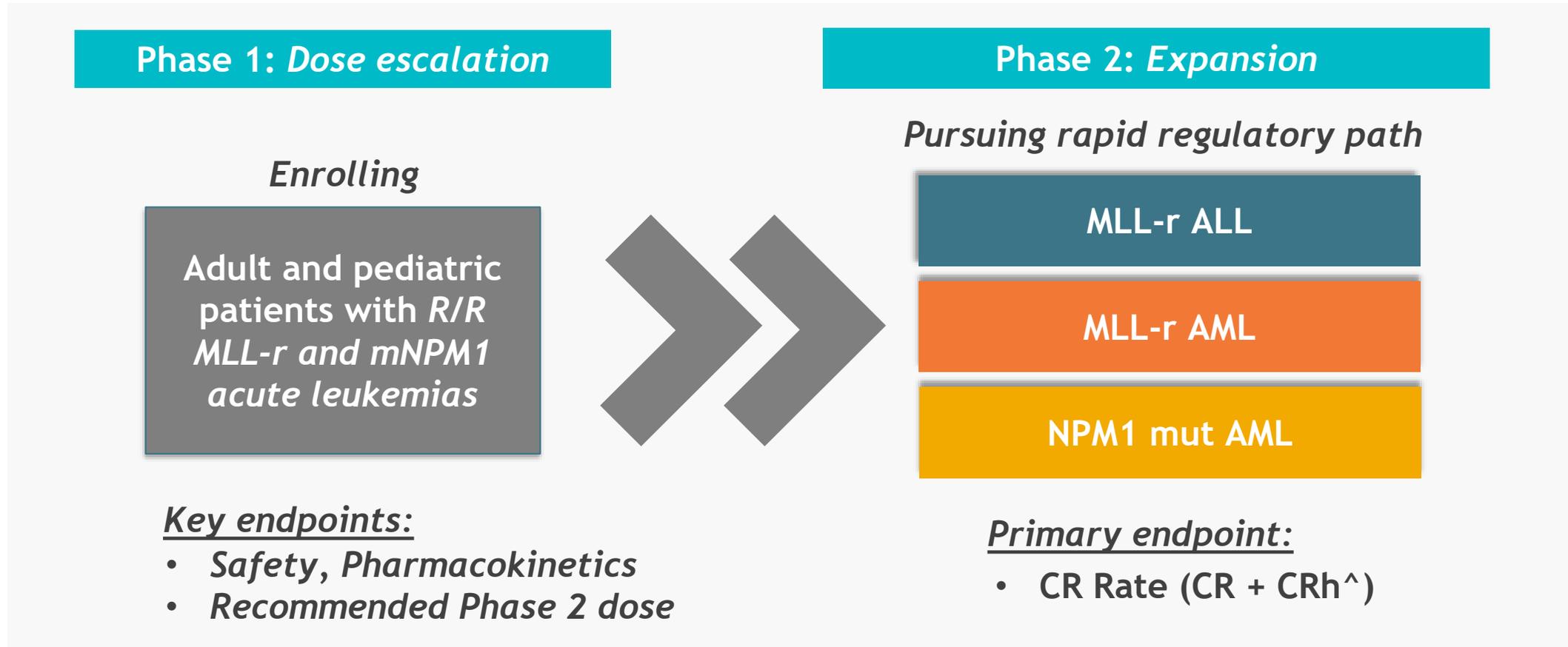
In Brief
Krivtsov et al. develop a selective and orally bioavailable small-molecule inhibitor targeting the Menin-MLL interaction, which suppresses a subset of MLL fusion target genes and significantly improves survival in PDX models of MLL-rearranged leukemia.

- 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
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<https://doi.org/10.1016/j.ccr.2019.11.001>



Syndax anticipates presenting data from AUGMENT-101 in early '21

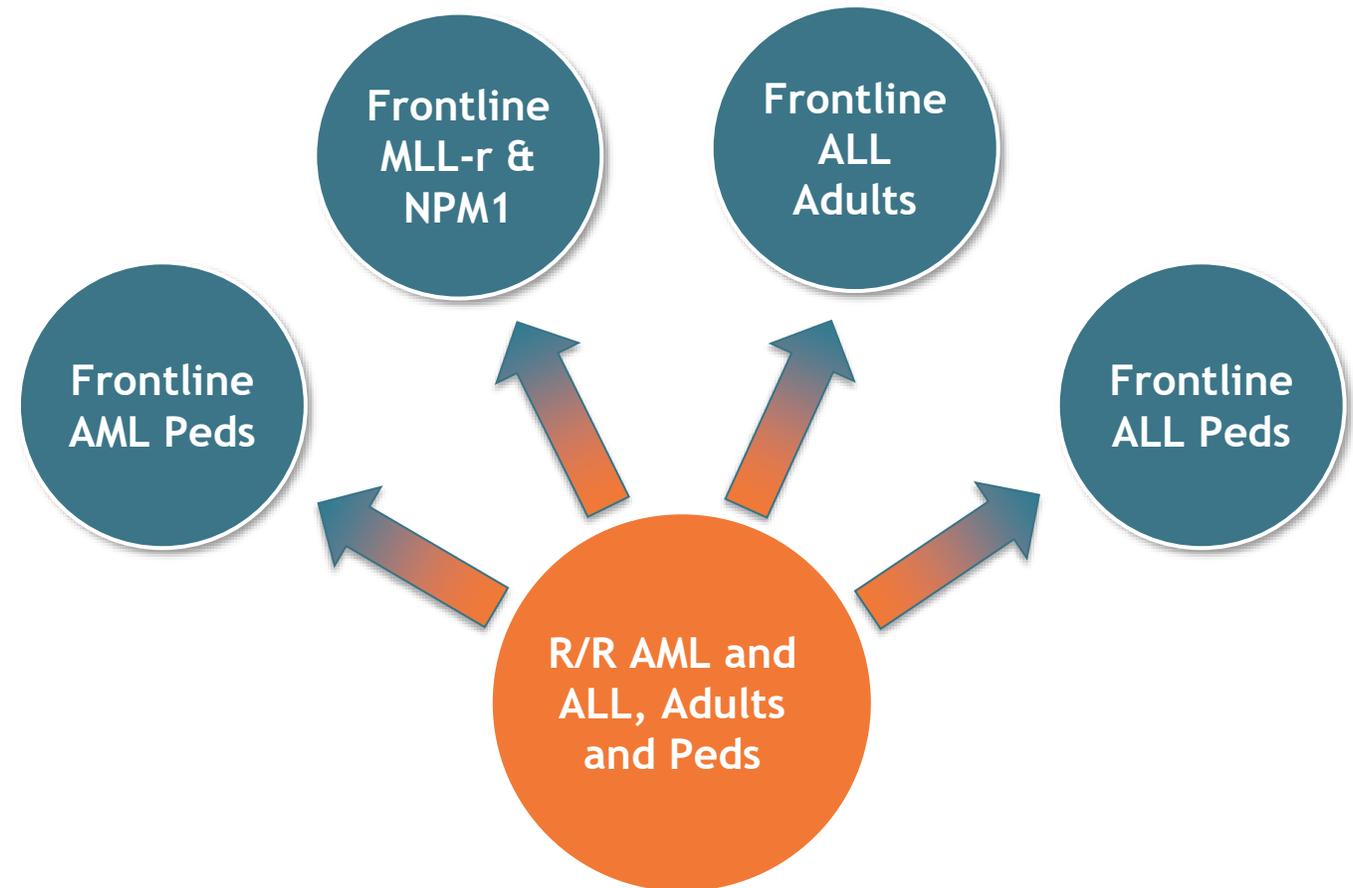


Initiation of Phase 2 anticipated in early 2021

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

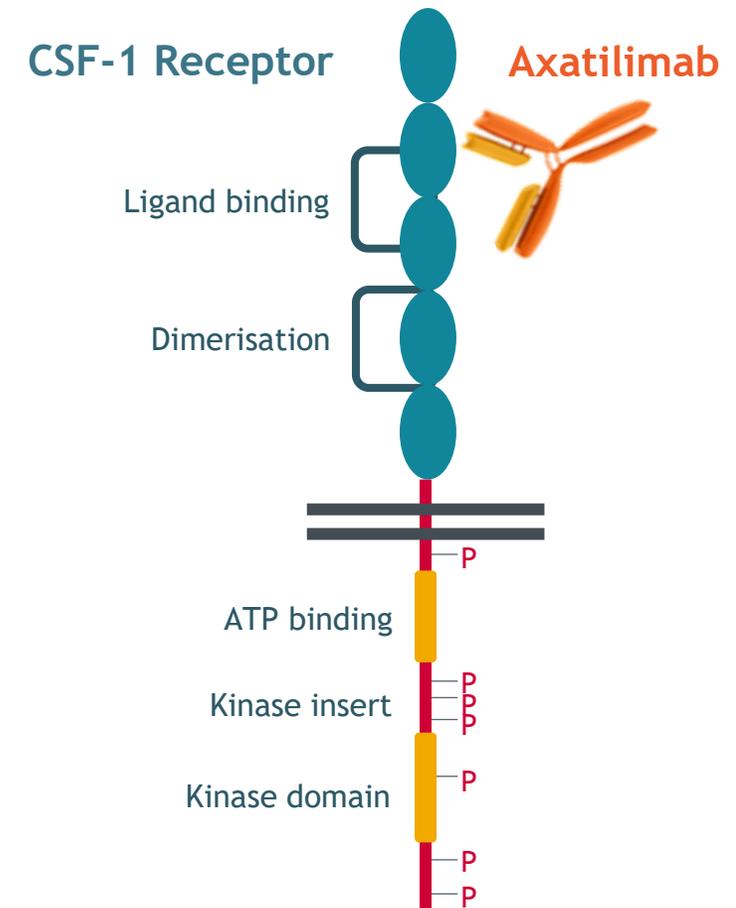
Multiple commercial opportunities in acute leukemias

- Fast to market regulatory path in R/R disease
- Subsequent approvals prioritized by medical need and commercial opportunity
- Collaborate and broaden utilization through combo and investigator-initiated trials



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

- Axatilimab Phase 1 data featured in oral presentation during ASH Virtual Meeting
 - ~15 patients with refractory cGVHD treated in Phase 1
 - Overall response rate and safety profile suggests compelling therapy for patients with cGVHD
- Inhibition of CSF-1R pathway significantly impacts fibrotic process



Efficacy and safety in cGVHD supports franchise opportunity in fibrotic diseases

AGAVE-201 is our global chronic GVHD pivotal trial

Inclusion criteria:

- 6 years and older
- Recurrent or refractory active cGVHD after at least 2 lines of systemic therapy



Primary Endpoint: Objective Response Rate (ORR) by 2014 NIH GVHD Criteria

Key Secondaries: Duration of response, Improvement in modified Lee Symptom Scale

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

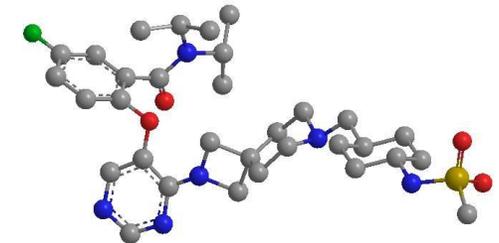
From UCB

Axatilimab



From Allergan/Vitae

Menin-MLL inhibitors



Financial highlights and 4th quarter financial guidance

Ticker	SNDX (NASDAQ)
Cash and short-term investments (at Sep 30, 2020)	\$170.2 million
Shares Outstanding* (at Nov 2, 2020)	44.4 million
4Q and 2020 Operating Expense Guidance	
	4Q 2020
Research and Development	\$15-20 M
Total Operating Expenses [^]	\$20-25 M

* Includes 40.8 million common shares and pre-funded warrants to purchase 3.6 million common shares;

[^] Includes ~\$2.0 million non-cash stock compensation expense per quarter

Thank you. Questions?

Syndax 