Presentation of Phase 1 data from the AUGMENT-101 trial

Syndax

APRIL 20, 2021

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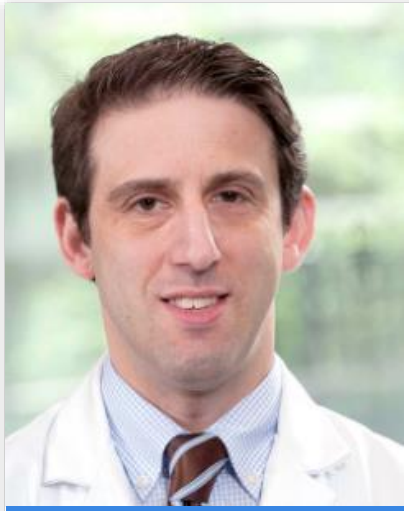
Today's guest speaker: Eytan Stein, MD



Memorial Sloan Kettering Cancer Center

AUGMENT-101 Principal Investigator (PI)

- Director of Program for Drug Development in Leukemia at Memorial Sloan Kettering Cancer Center (MSKCC)
- Led clinical studies of enasidenib & ivosidenib
- Led the trial of the DOT1L inhibitor pinometostat
- Extensive Phase 1 experience with novel compounds targeting IDH, PRMT5, DHODH, and Menin-MLL interaction
- Lead investigator at MSKCC for BEAT AML

Thank you to the patients, families and health care providers who have supported AUGMENT-101

WELCOME TO A SYNDAX-SPONSORED TRIAL

Thank You for volunteering to participate in this clinical study. We understand that deciding on a treatment option is difficult and that enrolling in a clinical trial is an important choice. We deeply appreciate your participation. The employees at Syndax are committed to discovery and development of new medicines to help people live longer, healthier lives. Without volunteers like you, we would be unable to conduct the rigorous clinical studies needed to develop new therapies.

We know time is of the essence during cancer treatment, and our team at Syndax is dedicated to working as quickly as possible to help people living with cancer. We have committed to making sure your involvement in this trial will be as simple and smooth as possible.

As a clinical trial participant, you may be interested in learning about the overall results of the trial once it has completed. Syndax is committed to expanding knowledge about new therapies and will publicly share results from this trial when they become available.

Thank you again,

Briggs Morrison
Syndax CEO
and the Syndax clinical trials team

clinicaltrials@syndax.com

Syndax

Phase 1 clinical trial sites

- Memorial Sloan Kettering Cancer Center
- The University of Texas MD Anderson Cancer Center — Making Cancer History®
- City of Hope
- Florida Cancer Specialists & Research Institute
- At the Forefront UChicagoMedicine Comprehensive Cancer Center
- Washington University in St. Louis
- Emory Winship Cancer Institute — National Cancer Institute-Designated Comprehensive Cancer Center
- Dana-Farber Cancer Institute

Positive initial Phase 1 results establish SNDX-5613 as the leading Menin-MLL interaction inhibitor

Well-tolerated

- No discontinuations for drug-related AEs
- Well tolerated through multiple cycles

Clear Evidence of Single Agent Activity

- Overall response rate*: 15/31 (48%)
  - 10/15 (67%) CR_{MRD-}

PK / PD, RP2D

- Dose meeting RP2D criteria identified
- Robust gene expression changes confirm MOA

** Overall response rate includes CR + CRh + CRp + CRi + MLFS observed among pts enrolled with MLLr or NPM1c Acute Leukemia*

SNDX-5613 Phase 1 AUGMENT-101

Eytan Stein, MD

No FDA-approved targeted therapies to treat MLLr or NPM1c acute leukemias

MLLr Acute Leukemias

Annual global incidence 5,000 - 7,000

4-10% AML

10-15% ALL

(80% of infant ALL)

- **5-year OS for Adult MLLr <25%**

NPM1 Mutant AML

Annual global incidence ~20,000

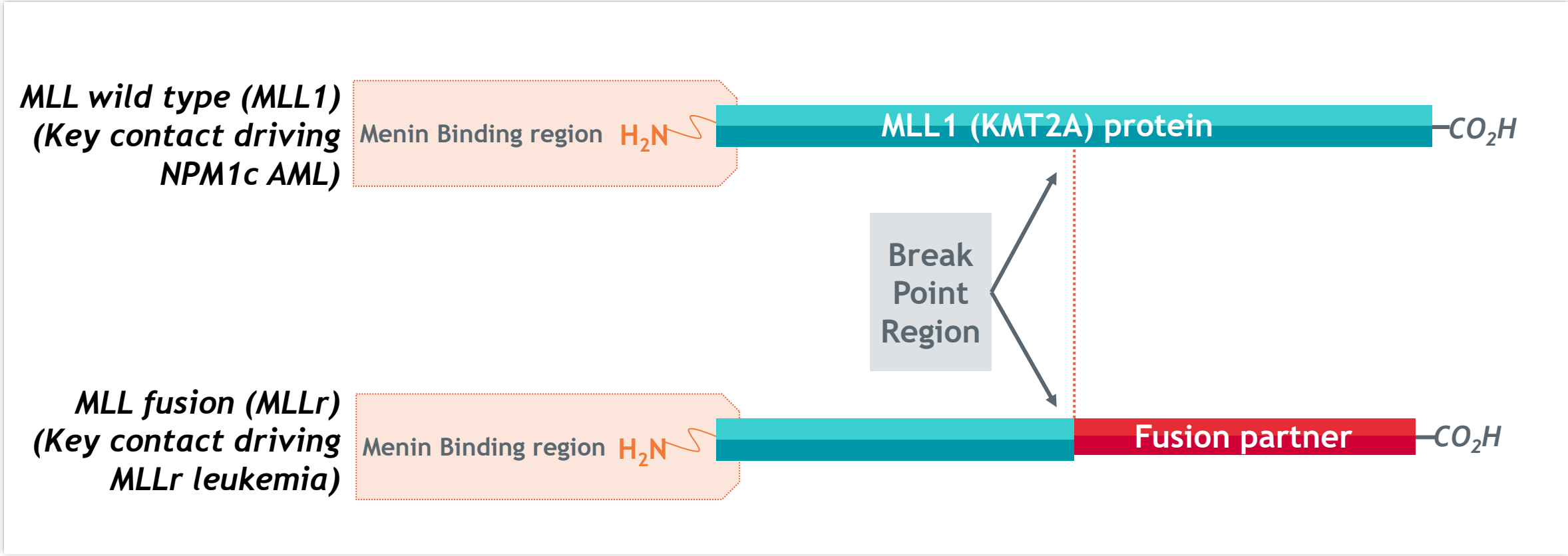
30% AML

- **5-year OS for Adult NPM1c AML 50%**
- **Known NPM1c co-mutations offer rational combination approaches**

Both MLLr and NPM1 acute leukemias are readily diagnosed

Sources: NCCN conference and meetings: NCCN guidelines; Dohner, H. et al. *Blood*, 2017; 129(4):424-447; Falini, B. et al. *Blood,* 2011; 117(4): 1109-1120;
MLLr = mixed lineage leukemia rearranged; NPM1c = mutant nucleophosmin 1

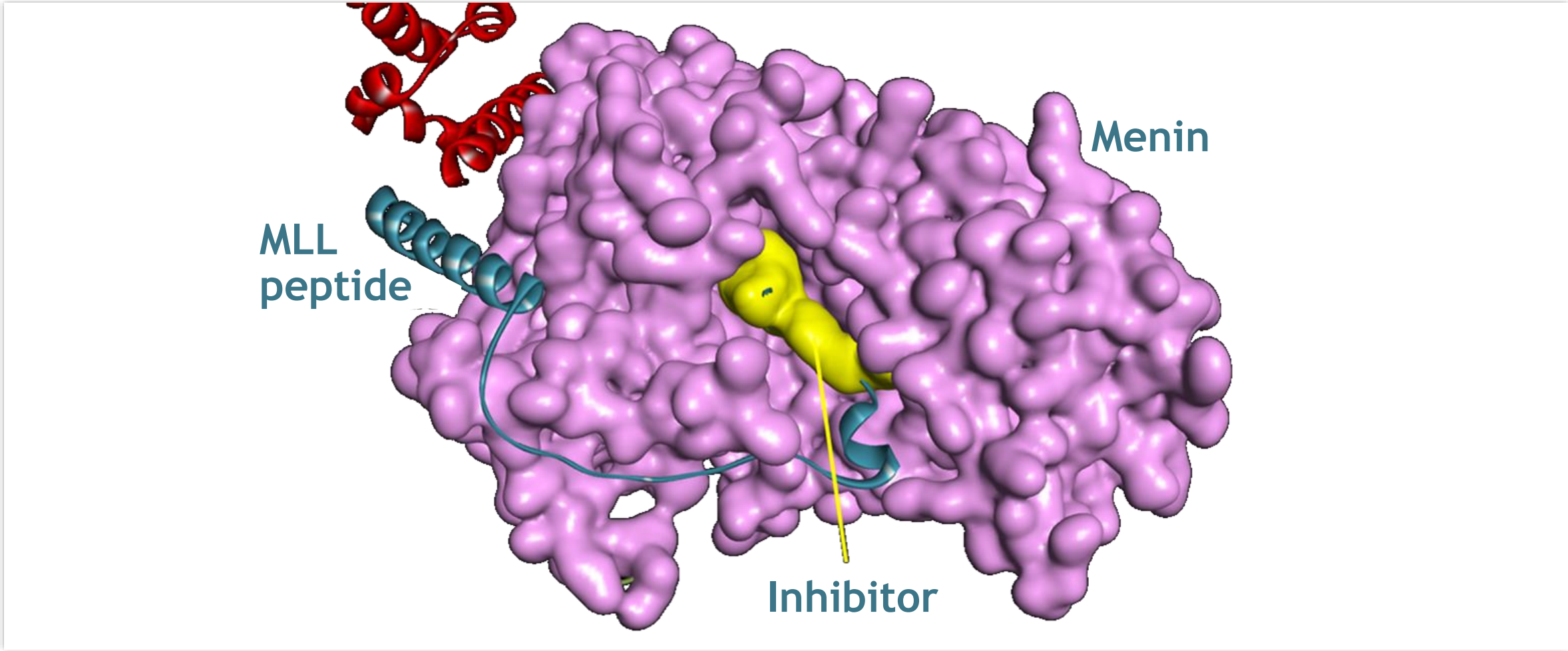
In MLLr and NPM1c, leukemic transformation is highly dependent on Menin-MLL interaction



MLL N-terminus binds within conserved pocket on Menin and serves as a key driver of NPM1c and MLLr acute leukemia[1]

Source: Yokoyama A, Cell. 2005 Oct 21;123(2):207-18; Caslini C, *Cancer Res. 2007* Aug 1;67(15):7275-83.

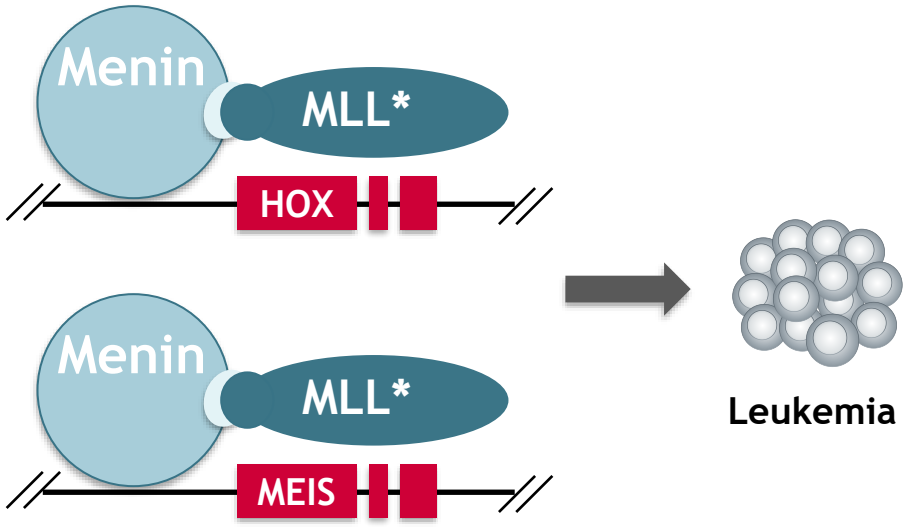
SNDX-5613 designed to block the site of Menin-MLL interaction



Menin is a scaffold protein involved in gene transcription

SNDX-5613 turns off leukemic transcriptional programs by binding to Menin and displacing MLL complexes

MLLr or NPM1c Acute Leukemias



Gene transcription ON

MLL* = MLLr or MLL1 wildtype; Adopted from: Uckelmann HJ, et al. Presented at ASH Annual Meeting, 2018

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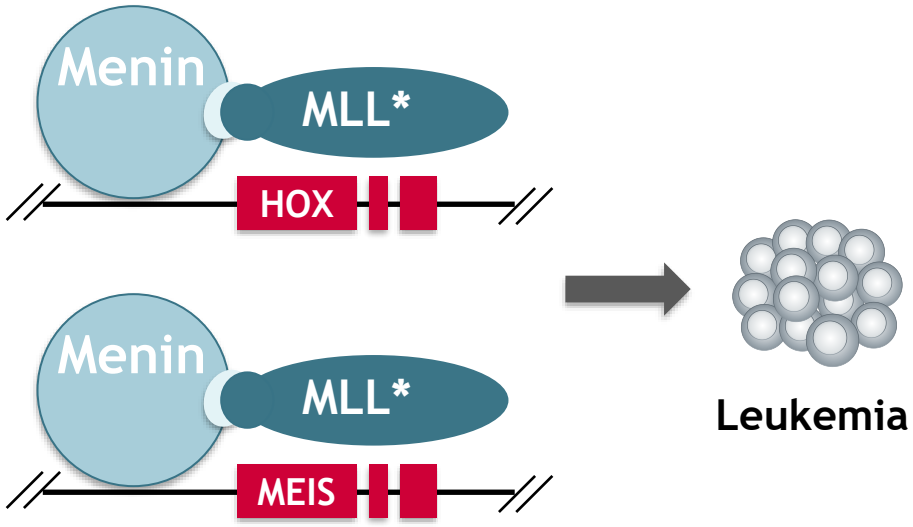
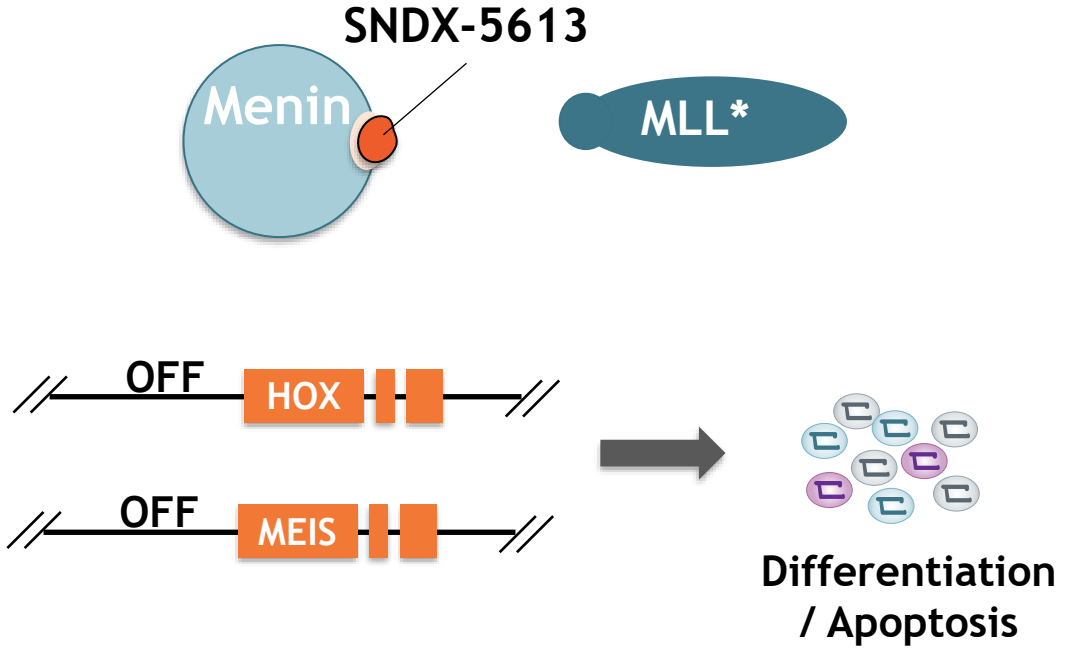


Gene transcription ON

Menin inhibition with SNDX-5613



Gene transcription OFF

MLL* = MLLr or MLL1 wildtype; Adopted from: Uckelmann HJ, et al. Presented at ASH Annual Meeting, 2018

Evolution of AUGMENT-101 based on emerging data and FDA input

Phase 1: *Dose escalation*

Trial at initiation

- Enrolled “all comers” R/R acute leukemia
- Oral, q12h continuous dosing of SNDX-5613
- Accelerated titration into a 3+3

Trial updates

- Separated pts by CYP3A4 use:
  - Arm A (not on strong CYP3A4)
  - Arm B (strong CYP3A4)
- Amended to enroll adult and pediatric* pts with MLLr or NPM1c acute leukemia
- Added ability to backfill cohorts if dose level cleared & responses observed

Key Endpoints: Safety, PK, RP2D

** Allows patients ≥ 30 days of age; MLLr = mixed lineage leukemia rearranged; NPM1c = mutant nucleophosmin 1*

AUGMENT-101 was carefully designed to select RP2D

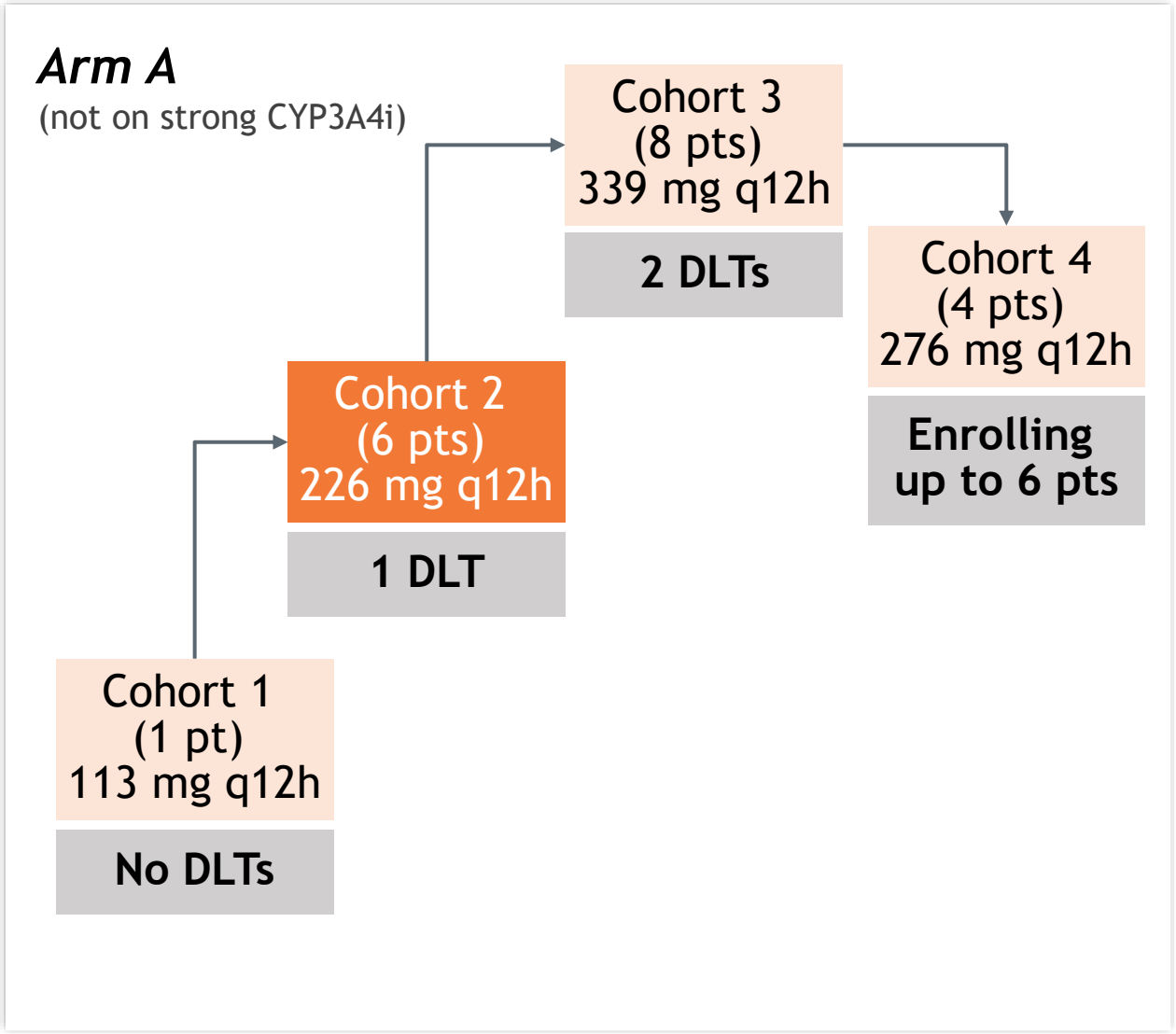
Prespecified RP2D determination criteria:

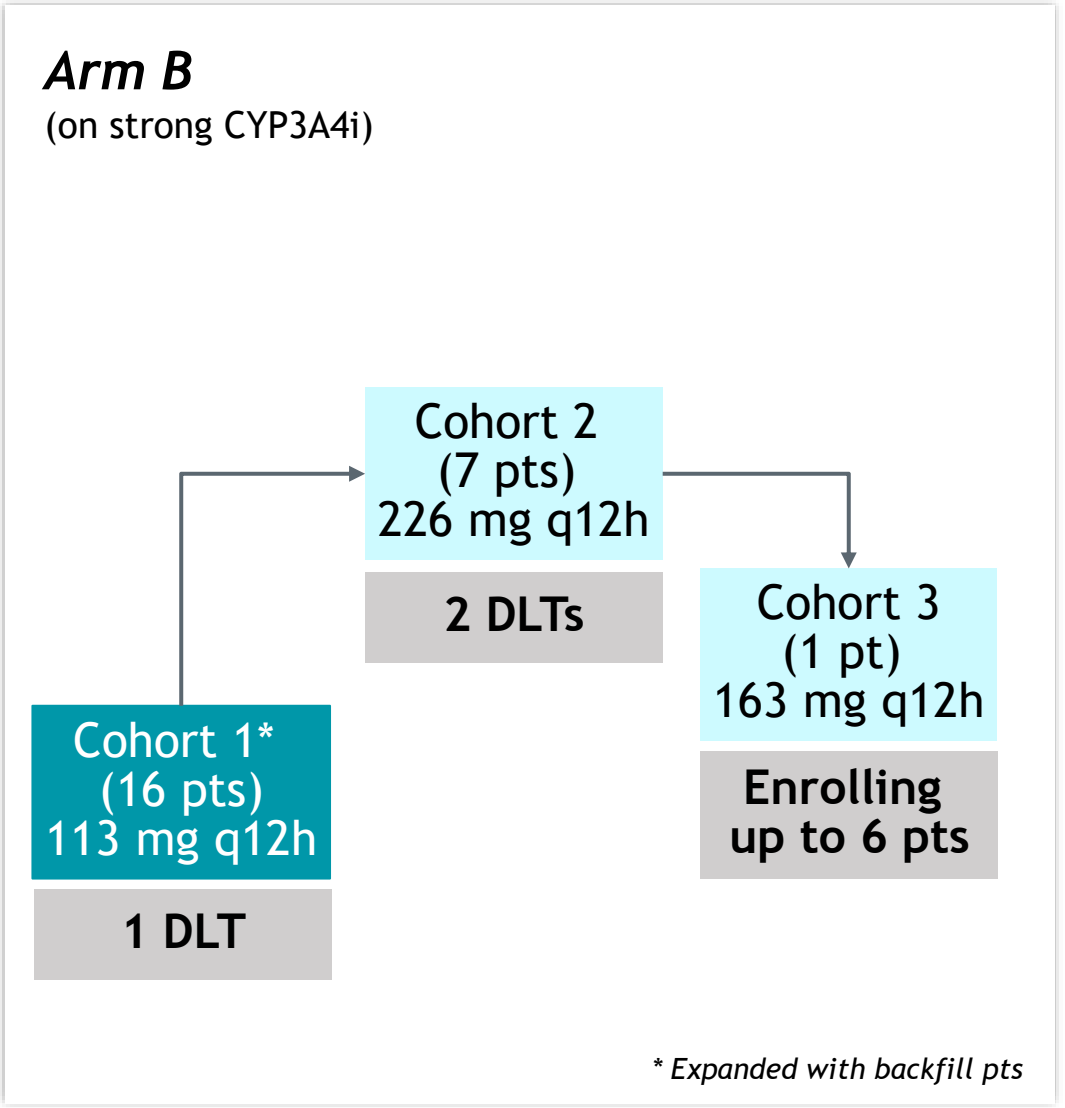
No more than 1 of 6 of evaluable patients experience a DLT

At least 2/3 of patients receive ≥ 80% of their dose in cycle 1 and cycle 2

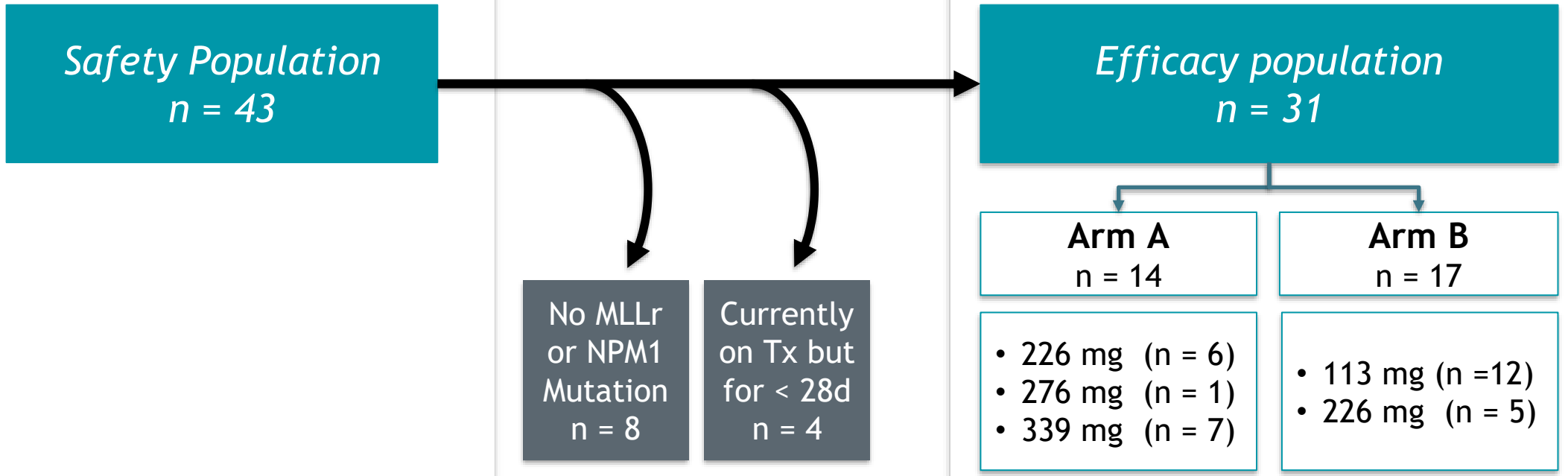
24-hour AUC (AUC_{0-24}) exceeds 15,000 ng×hr/mL in at least 2/3 of patients

We have rapidly identified a dose that meets our RP2D criteria





We have defined populations for safety and efficacy analyses



Safety population:
R/R Acute Leukemia patients who received ≥ 1 dose of SNDX-5613 at the time of the data cut-off

Efficacy evaluable pop:
MLLr or NPM1c pts completed DLT period or discontinued early due to death or progression

SNDX-5613 Phase 1 patients are heavily pre-treated and have a poor prognosis

Baseline Characteristics	Overall n=43
Median age, years (range)	54 (16, 78)
Female, n (%)	25 (58)
ECOG baseline performance (0/1/2), n (%)	9 (21) 31 (72) 2 (5)
Genetics of enrolled pts, n (%)	
MLLr	26 (61)
NPM1c	9 (21)
Non MLLr/Non NPM1c	8 (19)

Baseline Characteristics	Overall n=43
Leukemia Type, n (%)	
AML	34 (79)
ALL	8 (19)
MPAL	1 (2)
Median prior therapies (range)	3 (1,11)
Stem cell transplant, n (%)	16 (37)
Venetoclax	25 (58)
Targeted Therapy	9 (21)

Datacut: 12Mar2021

No discontinuations for treatment related AE, and 4 went on to HSCT

Patient Disposition	Safety Pop n = 43
Ongoing Patients, n (%)	**9 (21)**
Discontinued Treatment	**34 (79)**
Progressive Disease	15 (44)
Adverse Event (all unrelated)	8 (24)
Transplant	4 (12)
Death	3 (9)
Withdrew Consent	2 (6)
Physician Decision	1 (3)
Other	1 (3)
Treatment-Related Adverse Event	0

HSCT = hematopoietic stem cell transplant

Datacut: 12Mar2021

SNDX-5613 was well-tolerated across all doses

Gr 1 or 2 treatment related AE (>2%)	Overall n = 43	
	Gr 1	Gr 2
Pts with ≥1 treatment related AE, n(%)	25 (58)	17 (40)
ECG QT prolonged	8 (19)	8 (19)
Hyperphosphatemia	-	3 (7)
Nausea	5 (12)	3 (7)
Vomiting	5 (12)	3 (7)
Diarrhea	4 (9)	-
Decreased appetite	-	2(5)
Differentiation syndrome	1 (2)	2(5)
Fatigue	-	2 (5)
Dysgeusia	2 (5)	-
Edema peripheral	2 (5)	-

≥Gr 3 treatment related AE	Overall n = 43
Pts with ≥Gr 3 treatment related AE, n(%)	**10 (23)**
ECG QT Prolonged	6 (14)
Anemia	2 (5)
Differentiation syndrome	2 (5)
Asthenia	1 (2)
Cellulitis	1 (2)
Diarrhea	1 (2)
Fatigue	1 (2)
Hypokalemia	1 (2)
Leukocytosis	1 (2)
Platelet count decreased (Gr 4)	1 (2)

Clinical AE profile consistent with highly selective menin inhibition

Datacut: 12Mar2021

Treatment goals for patients with relapsed/refractory acute leukemia

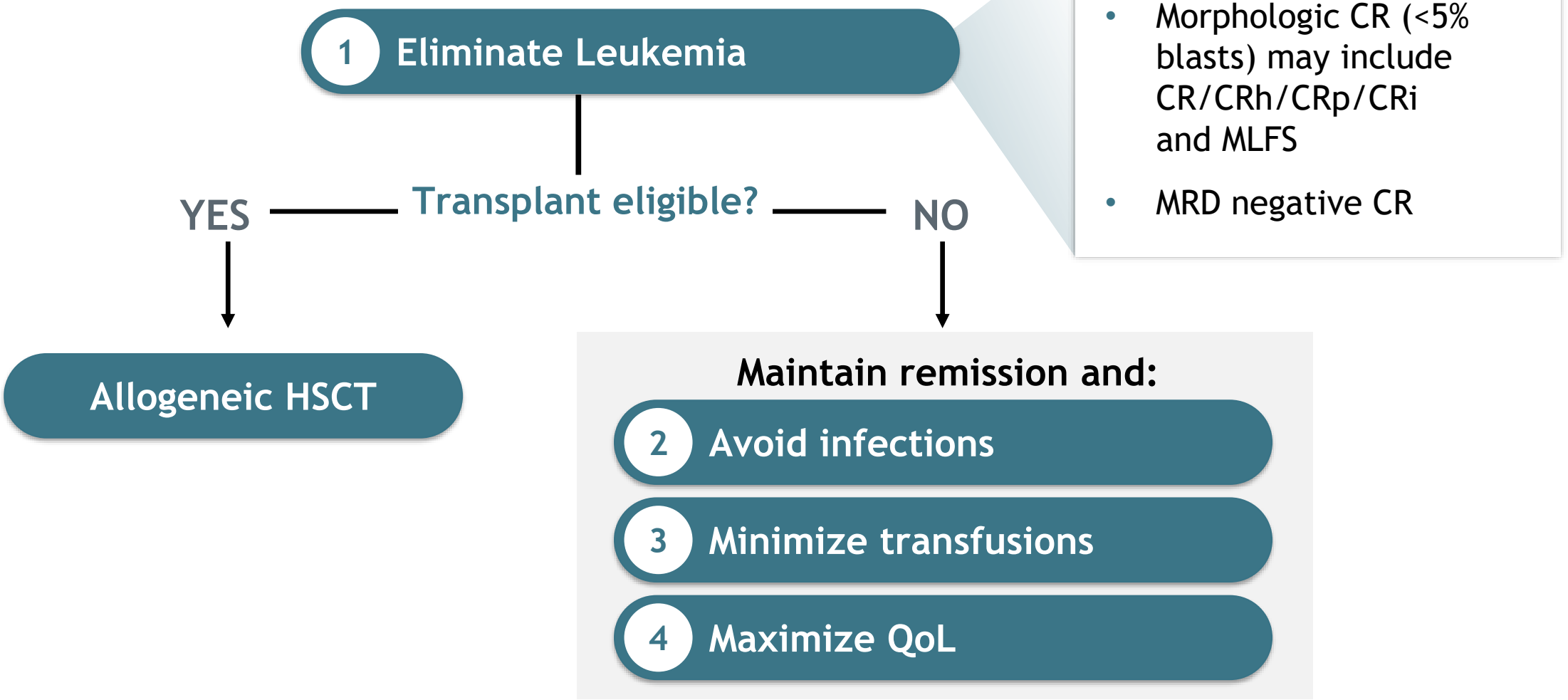
1 Eliminate Leukemia

Defined by:

- Morphologic CR (<5% blasts) may include CR/CRh/CRp/CRi and MLFS
- MRD negative CR

CR = normal blood counts; no transfusion; CRh = ANC >500, >50K Platelets; no transfusion; CRp = ANC >1000, Platelets <100K; no transfusion; CRi = ANC < 500; MLFS = clearance of blasts without blood count recovery that meets the criteria for CRh or CR

Treatment goals for patients with relapsed/refractory acute leukemia



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SNDX-5613 demonstrated promising anti-leukemic activity in patients with relapsed/refractory MLLr and NPM1c leukemia

Best Response at data cutoff	Response Evaluable n = 31 (%)
Overall Response Rate*	**15/31 (48%)**
CR/CRh	5
CRp	5
CRi/MLFS	5
MRD negative^ ORR	10/15 (67%)
MLLr overall response rate	13/24 (54%)
mNPM1 overall response rate	2/7 (29%)

4 MRD- patients went on to receive stem cell transplant

** Overall Response Rate = CR + CRh + CRp + CRi + MLFS; ^ MRD status assessed locally by PCR or Flow*

Datacut: 12Mar2021

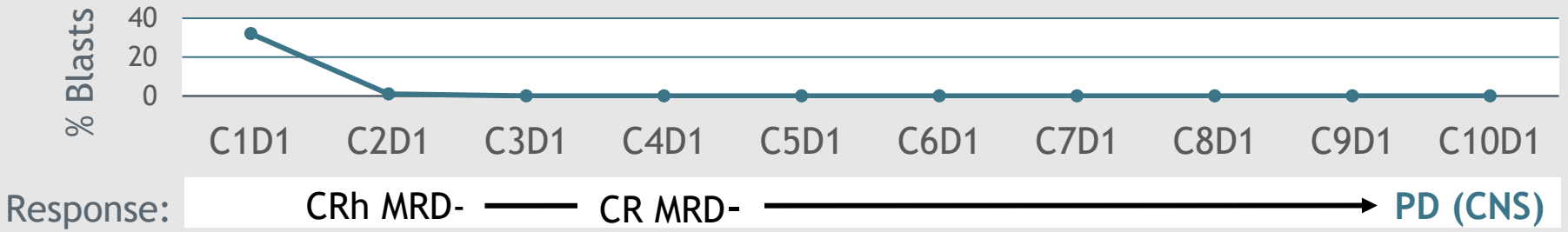
Promising anti-leukemic activity observed across patient subsets

- Responses observed in AML and ALL
- Responses observed in Arm A and Arm B
- Responses observed in 8 of 16 (50%) who underwent prior SCT
- Responses observed in 9 of 25 (36%) who received prior venetoclax

Datacut: 12Mar2021

Patient with MPAL (MLLr) sustained CR after one cycle

69 y.o.
female
MPAL-MLLr



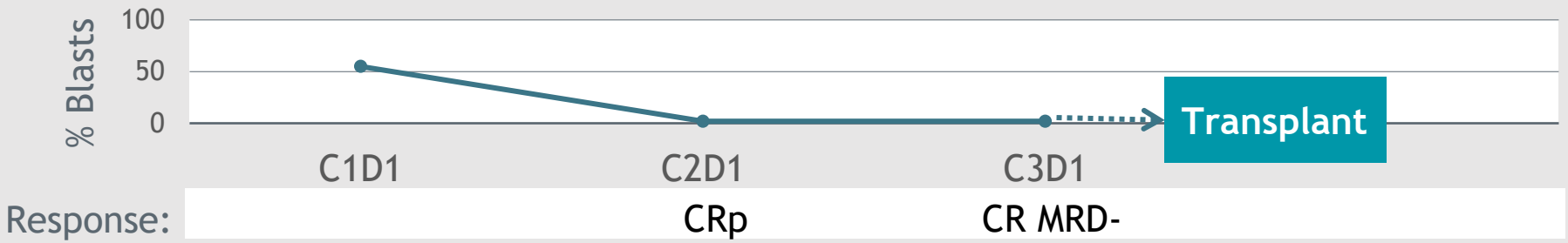
Demographics	69 y.o., female	
Diagnosis	MPAL-MLLr; T(V;11Q23), FLT3	
Prior regimens and response	HiDAC/MVD Gilteritinib	1 mo - PR 5 mo - CR
SNDX-5613 Dose	226mg q12h + Posaconazole	
Dose reduction	Day 17 Grade 2 prolonged QTc, dose reduced to 113mg q12h	
Response	Patient completed 9 cycles with CRh MRD- by cycle 2	

Death due to CNS recurrence with no signs of bone marrow recurrence

BM, bone marrow; CNS, central nervous system; CR, complete response; HiDAC, high-dose Ara-C; MPAL, mixed phenotype acute leukemia; MRD, minimal residual disease; MVD, mitoxantrone vincristine dexamethasone; ND, not done; PD, progressive disease; PR, partial response.

Patient with AML (MLLr) transplant eligible after 3 cycles

66 y.o. female AML-MLLr



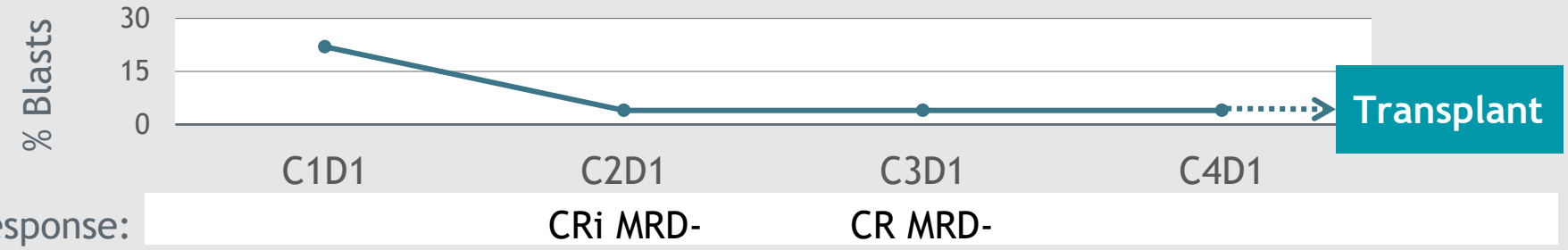
Demographics	66 y.o., female	
Diagnosis	AML-MLLr t(11;17)(q23;q12)	
Prior regimens and response	Cytarabine/daunorubicin Fludarabine/busulfan + HSCT Entospletinib	CR CR Refractory
SNDX-5613 Dose	339mg q12h (no CYP3A4i)	
Dose reduction	Day 4 Grade 3 prolonged QTc, dose reduced to 226mg q12h	
Response	CRp by cycle 2 day 1, converted to CR MRD- by cycle 3 and went on to transplant	

Patient received transplant on study day 88

AML, Acute myeloid leukemia; CR, Complete Response; MLLr, mixed lineage leukemia rearrangement; CRp, Complete Response incomplete platelet recovery; CRi, Complete Response incomplete hematologic recovery; q12h, every 12 hours.

Patient with AML (NPM1c / IDH1^{mut}) achieves CR after two cycles

30 y.o. female NPM1c

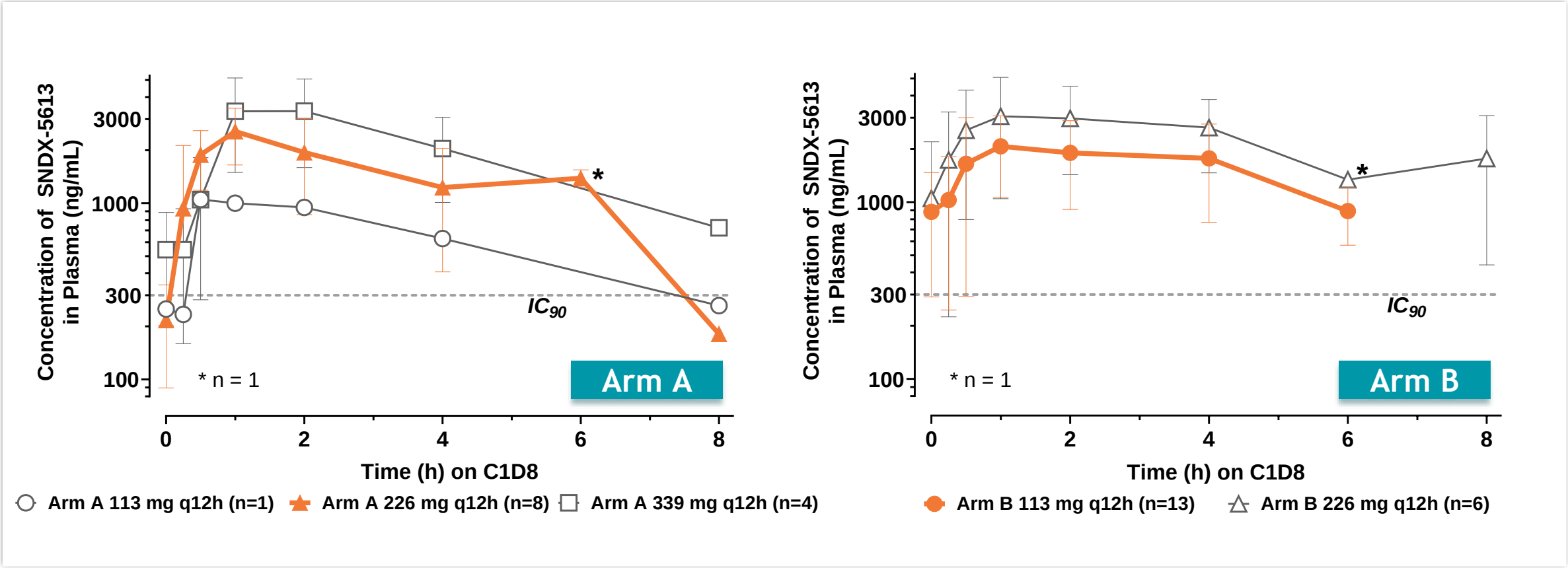


Demographics	30 y.o., female	
Diagnosis	Treatment related AML (NPM1c/IDH1^{mut}) (Stage IIB Breast Cancer July 2016)	
Prior regimens and response	Daunorubicin and Cytarabine (Vyxeos™)	Refractory
SNDX-5613 Dose	113mg q12h + Posaconazole	
Dose reduction	None	
Response	CRi MRD- at C2D1, converted to CR MRD- on C3D1, and went on to transplant	

Patient went on to transplant after cycle 3

AML, Acute myeloid leukemia; ANC, absolute neutrophil count; CR, Complete Response; CRi, Complete Response incomplete hematologic recovery; IDH1: isocitrate dehydrogenase 1 gene; NPM1: nucleophosmin 1 gene; Plt, platelets; q12h, every 12 hours.

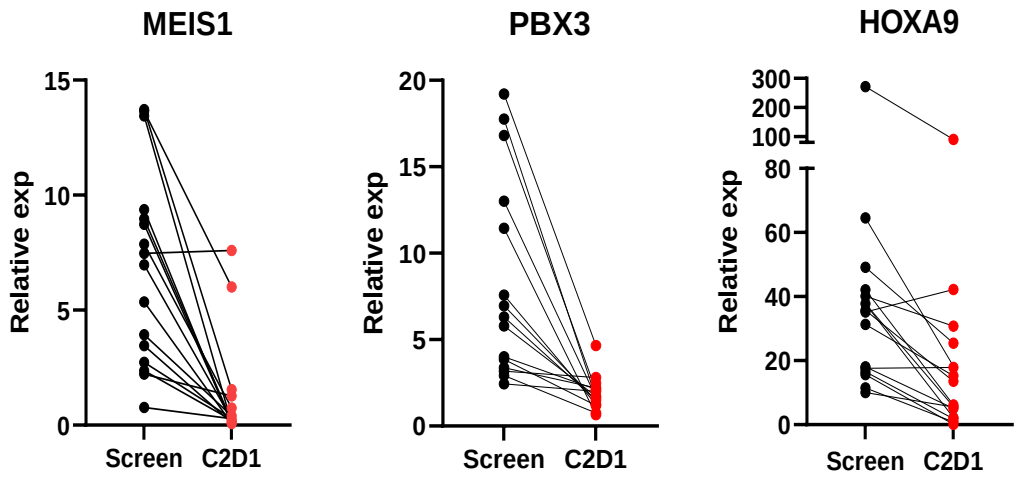
Dose proportional exposure achieved across both arms



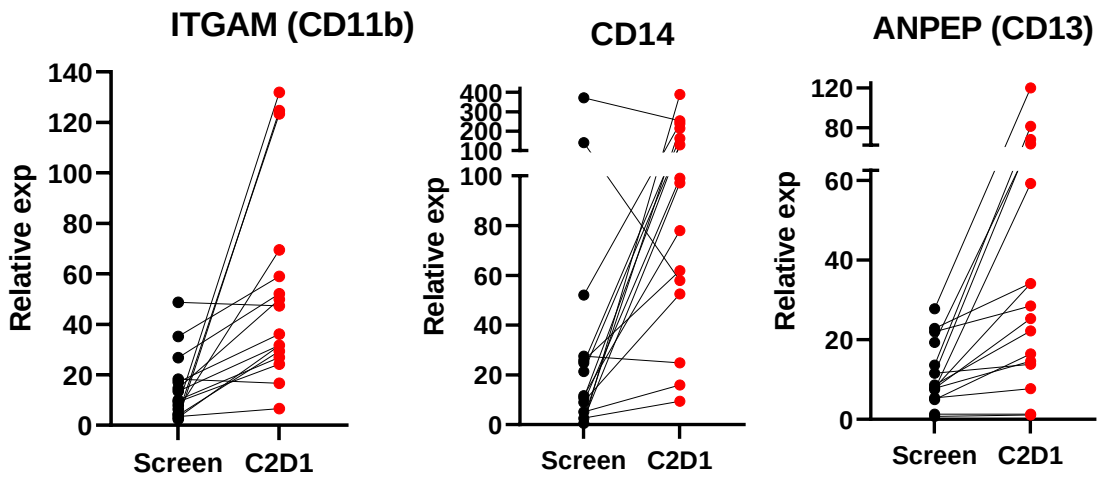
Steady-state levels achievable in ~2 days, no evidence of drug accumulation

SNDX-5613 pharmacodynamic activity confirms MOA

Down-regulated leukemogenic gene expression



Up-regulated differentiation markers



Gene expression measured by RNA-seq of bone marrow samples taken at screening and C2D1 (n=16)

Robust gene expression changes across arms, dose ranges and in both MLLr and NPM1

Dose from each arm meets prespecified selection criteria for advancing to Phase 2

226 mg q12h not on strong CYP3A4i and 113 q12h on strong CYP3A4i

- **No more than 1 of 6 of evaluable patients experience a DLT**
- **At least 2/3 of patients receive ≥ 80% of their dose in cycle 1 and cycle 2**
- **24-hour AUC (AUC_{0-24}) exceeds 15,000 ng×hr/mL in at least 2/3 of patients**

Adverse event and response results consistent with overall population
Grade 3 QTc 9%

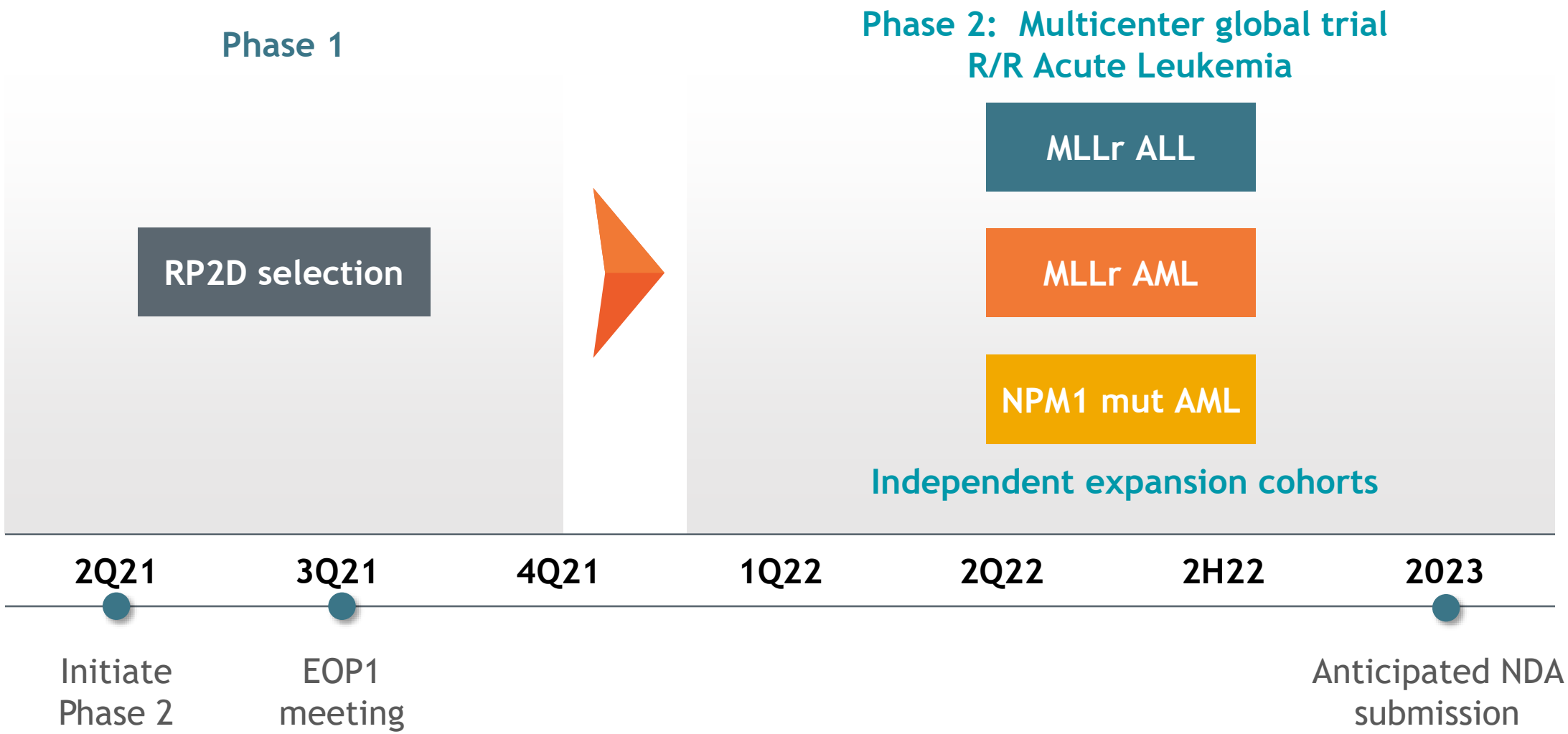
Conclusions

- Targeted therapy for MLL-rearranged and NPM1 mutant leukemias are desperately needed
- SNDX-5613 was a well tolerated oral therapy with a favorable adverse event profile
- Criteria have been met to establish the recommended Phase 2 doses
- Pharmacodynamic data show target engagement and down-regulation of leukemia-causing gene expression
- Evidence of single agent anti-leukemic activity with an ORR of 48% and 67% of responders achieving MRD- status, compares favorably with other agents available for R/R AML
- Phase 1 results in R/R population strongly support moving SNDX-5613 into Phase 2 and earlier lines of treatment

Broadening use of SNDX-5613 in acute leukemias

Briggs Morrison, MD

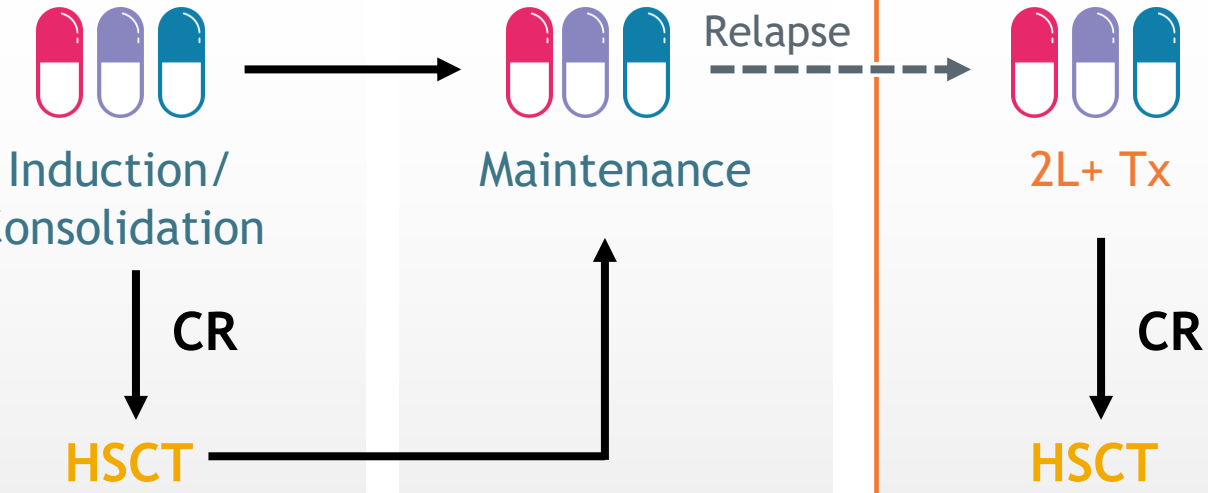
Anticipate initiation of Phase 2 expansion mid-2021



Redefining the MLLr/NPM1c acute leukemia patient journey

Primary treatment goals

1. Increase CR rate
2. Increase pts going to HSCT
3. Increase time in remission



	Induction/ Consolidation	Maintenance	2L+ Tx
Duration of treatment	Fit: 2 - 6 mo Unfit: ~12 mo	12 – 36 Mo	6+ mo
Response rates	MLLr: mod - high NPM1c: high	MLLr: low NPM1c: mod	MLLr: very low NPM1c: low

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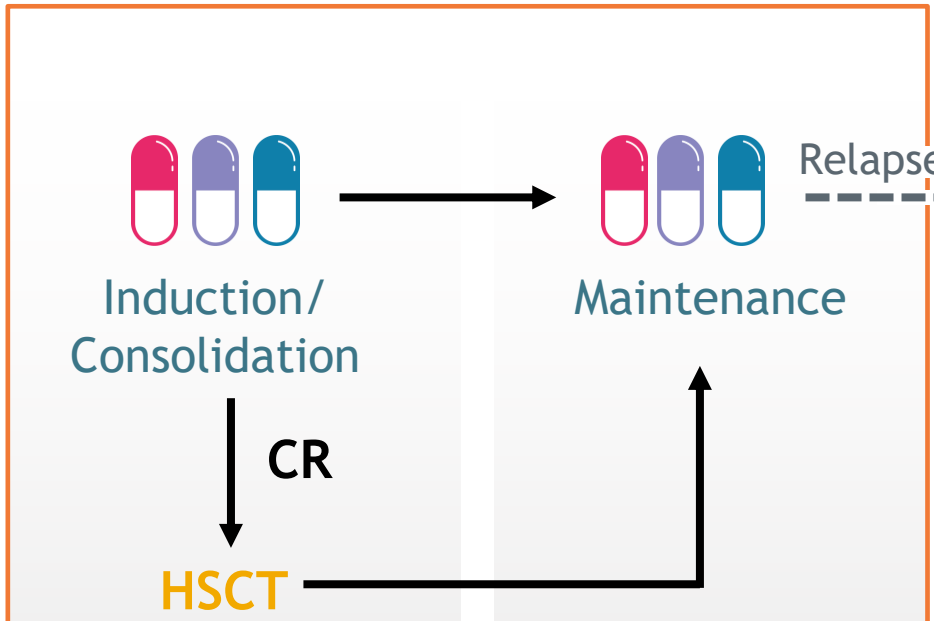

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SNDX-5613 has first- and best-in-class potential in diseases with significant unmet need

First / Best-in-class

- Candidate RP2D identified
- Pivotal trial anticipated in 2Q21; potential filing 2023
- Clear evidence of robust anti-leukemic activity in R/R NPM1c and MLLr
- Well tolerated through multiple cycles

Defined dev. strategy

- Potential approval in adult and pediatric R/R MLLr and NPM1c acute leukemia
- Front line and maintenance trials planned in both NPM1c and MLLr acute leukemia

Significant need

- No approved therapies targeting MLLr or NPM1c acute leukemias
- MLLr and NPM1 annual global incidence >25,000 pts

Thank you. Questions?

Syndax