Pipeline Update

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October 7, 2024

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TRADEMARKS

On Today's Call

Ahmed Hamdy, MD
Chief Executive Officer
Vincerx Pharma, Inc.

M. Yair Levy, MD
Director of Hematologic Malignancies Research
Texas Oncology

Today's Presentation

Topic	*Presenter*
Program Update: Enitociclib	Dr. Ahmed Hamdy
Program Update: VIP236	Dr. Ahmed Hamdy
Initial Phase 1 Dose Escalation Data for VIP943	Dr. Ahmed Hamdy
Discussion with Dr. M. Yair Levy	Dr. M. Yair Levy Dr. Ahmed Hamdy
Q&A	Dr. Ahmed Hamdy

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Phase 1 Dose Escalation Study in Collaboration with the National Institutes of Health

ONGOING; CURRENTLY RECRUITING DOSE LEVEL 3

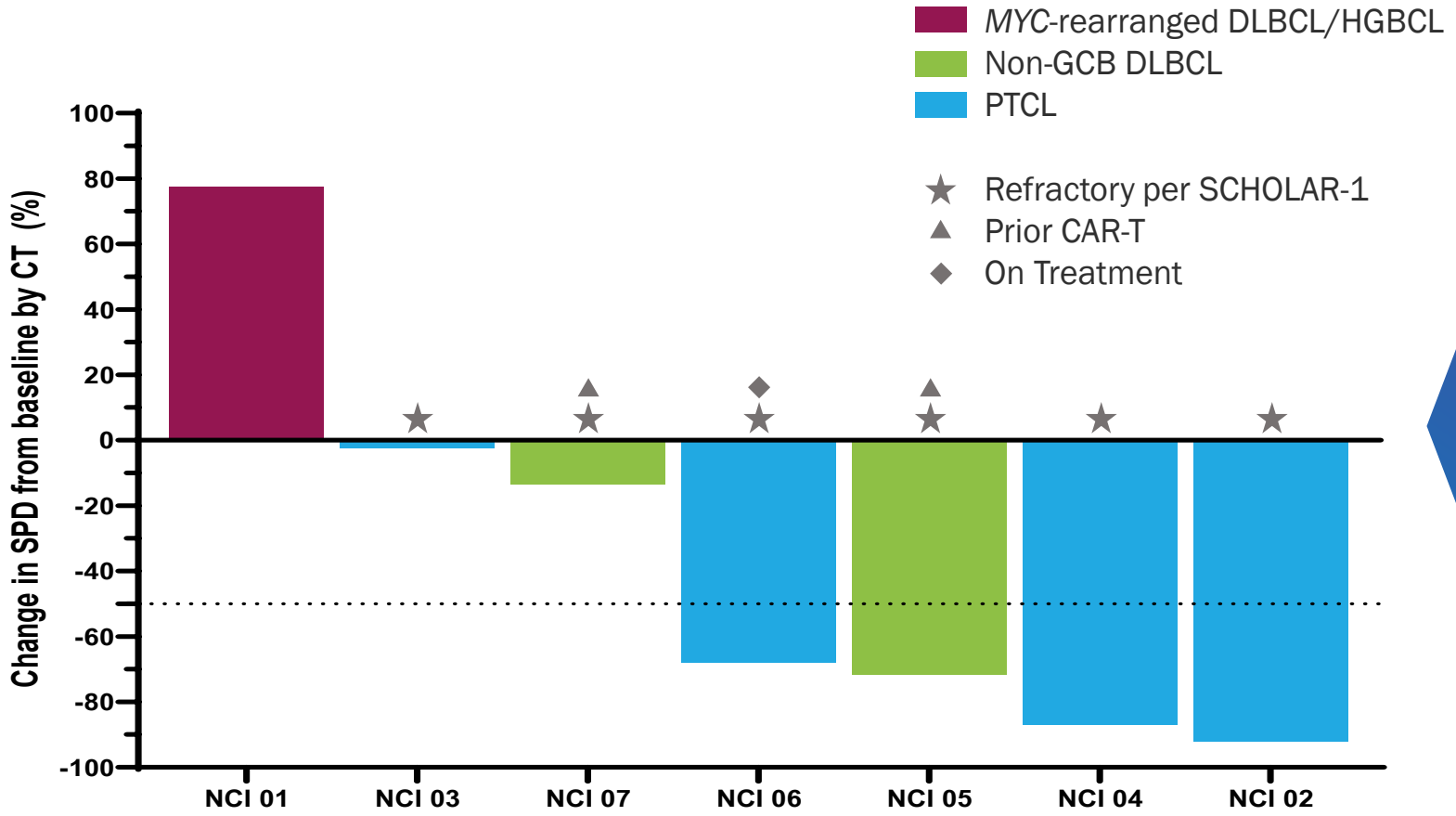
- Study Objectives:
  - Phase 1: To determine the maximum tolerated dose, recommended phase 2 dose, and the safety and toxicity profile of the combination of VIP152 with venetoclax and prednisone (VVIP)
    - MYC-rearranged DLBCL
    - Non-GCB DLBCL
    - Peripheral T-cell lymphoma
  - Phase 2: To determine the complete response rate of the combination of VIP152 with venetoclax and prednisone

Dose Escalation Levels			
Dose Level	Dose of VIP152	Dose of Venetoclax	
1	15 mg IV on D2 & D9	600 mg PO daily 1-10	
2	22.5 mg IV on D2 & D9	600 mg PO daily 1-10	
3	30 mg IV on D2 & D9	600 mg PO daily 1-10	In Progress
4	30 mg IV on D2 & D9	800 mg PO daily 1-10	

VNC-152-801: VVIP in R/R Lymphoid Malignancies NCT05371054

Enitociclib In Combination with Venetoclax and Prednisone Induces Four Partial Responses

DOSE ESCALATION CONTINUES



- Patient with R/R AITL
  - 91% decrease in tumor burden
  - **Partial response on dose level 1**
- Patient with HGBCL-DH-BCL2
  - ~70% decrease in tumor burden
  - **Partial response on dose level 2**
- Patient with EBV+ PTCL
  - 80% decrease in pulmonary lesion
  - **Partial response on dose level 2**
- Patient with ALK-ALCL
  - Reduction in LNs and skin lesions
  - **Partial response on dose level 2**

Phase 1 Dose Escalation Study of Enitociclib Monotherapy Achieves Durable Complete Remissions

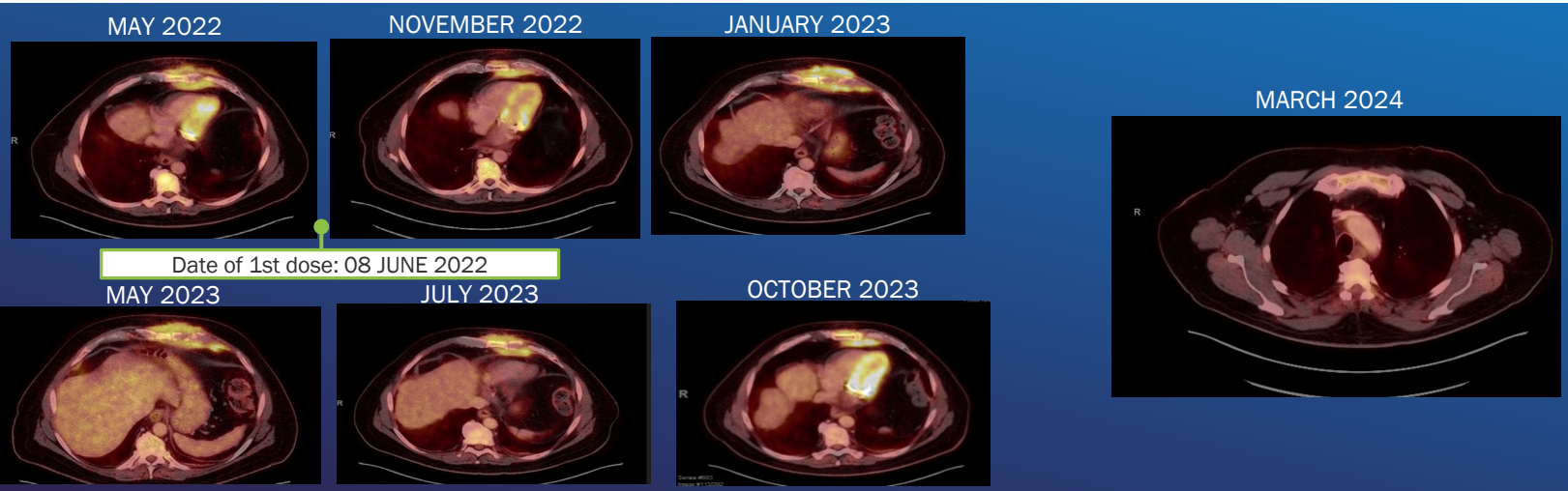
TREATMENT WAS WELL TOLERATED WITH ONE PATIENT STILL ON TREATMENT >26 MONTHS

- **2 CRs of 7 DH-DLBCL (29% CR rate)**
  - Both patients continue in full remission ~2 years after stopping treatment
- **13 patients with solid tumors had stable disease as best response**
- **1 patient with transformed follicular lymphoma achieved a Partial Response (PR)**
  - Best response was 65% tumor reduction (currently in cycle 39)
  - On treatment for >26 months

PATIENT: Diagnosis tFL

Age: 72 years
Cell of origin: GCB
Prior therapy (response):
- R-EPOCH (CR for 5 years)

Status: Active in Cycle 39
Latest Response: Partial Metabolic Response /PR



Data Extract: 13SEP24

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Differentiated and Favorable Safety in Dose Escalation Study

POSITIONS VIP236 AS A STRONG COMBINATION PARTNER

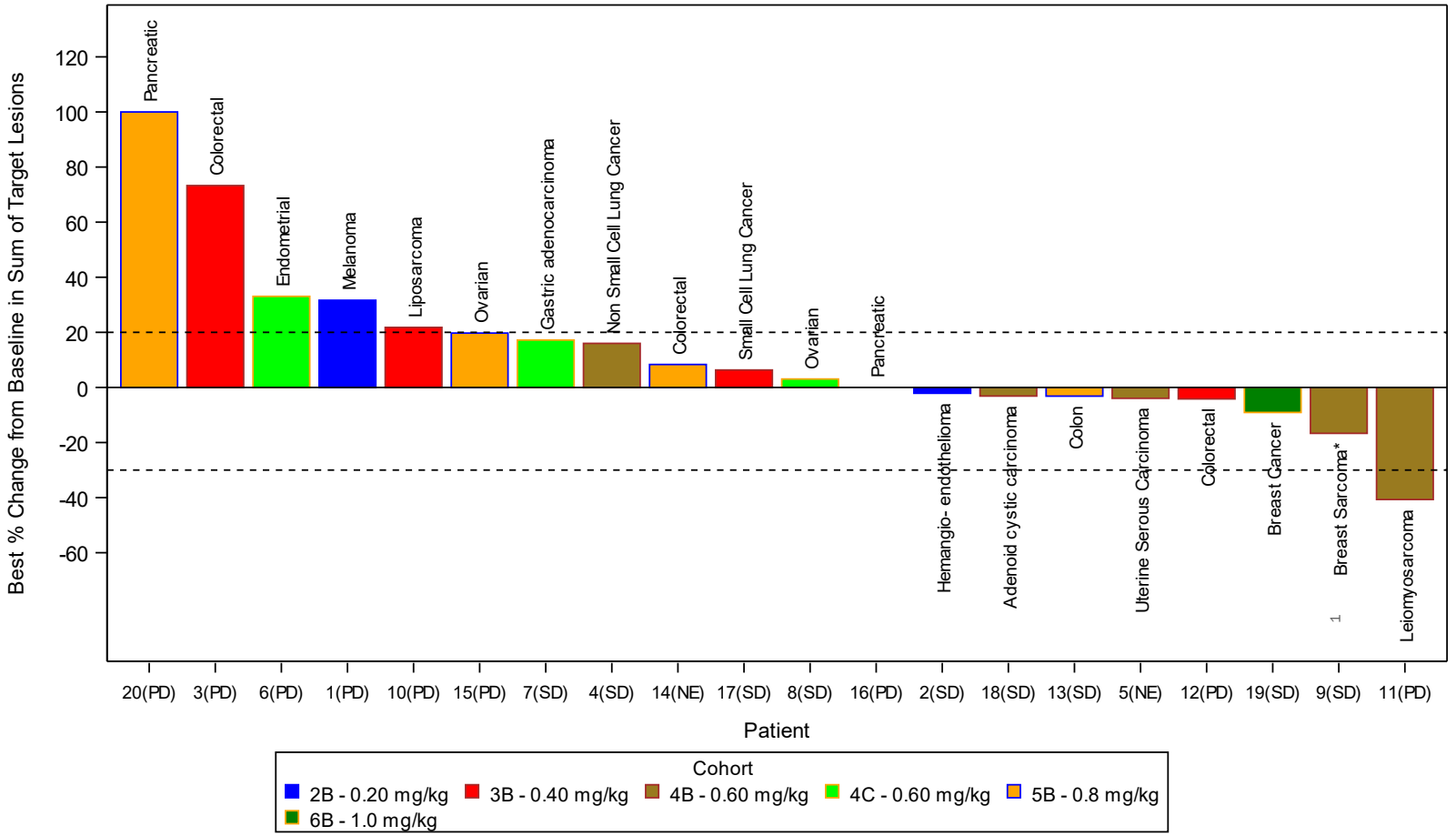
Drug-related Adverse Events		All Cohorts (2/5, Q3W, Q2W) (n=29)			
Preferred Term	ALL	G1	G2	G3	G4
Nausea	13 (44.8%)	12 (41.4%)	1 (3.4%)	0	0
Alopecia	11(37.9%)	4 (13.8%)	7 (24.1%)	0	0
Diarrhea	9 (31.0%)	8 (27.6%)	1 (3.4)	0	0
Fatigue	9 (31.0%)	5 (17.2%)	2 (6.9%%)	2 (6.9%)	0
Neutropenia	9 (31.0%)	0	1 (3.4%)	2 (6.9%)	6 (20.7%)
White blood cell count decreased	9 (31.0%)	0	1 (3.4%)	7 (24.1%)	1 (3.4%)
Vomiting	8 (27.6%)	5 (17.2%)	3 (10.3%)	0	0
Thrombocytopenia	8 (27.6%)	3 (10.3%)	2 (6.9%)	1 (3.4%)	2 (6.9%)
Anemia	6 (20.7%)	0	0	6 (20.7%)	0
Decreased appetite	4 (13.8%)	1 (3.4%)	2 (6.9%)	1 (3.4%)	0
Lymphocyte count decreased	4 (13.8%)	0	1 (3.4%)	2 (6.9%)	1 (3.4%)

- VIP236's optimized CPT payload successfully mitigates severe diarrhea, with no observed grade 3/4 cases in the study.
- Severe diarrhea is a common and serious adverse event seen with 1st and 2nd generation camptothecins.

Data taken from data cut – 04 SEP 2024
Unaudited data subject to change

Disease Control in Heavily Pretreated Patients

COHORTS 2b-6b (Q3W SCHEDULE) AND COHORT 4c (Q2W SCHEDULE); N=20 (EVALUABLE FOR CT-SCAN)



DISEASE CONTROL (STABLE DISEASE) IN 45% OF EVALUABLE PATIENTS, PER PROTOCOL

*Still on study

[1]The leiomyosarcoma patient had a 41% decrease in two target lesions, but a new 2cm lesion was detected at first scan

Unaudited data; subject to change

Data Extract: 04SEP24

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VIP236 Positioned as Strong Agent for Combination Therapies

PURSUING STRATEGIC PARTNERSHIPS TO CHAMPION FUTURE DEVELOPMENT

FIRST AND SECOND-GENERATION CAMPTOTHECINS

- Camptothecin-derived therapies have been a cornerstone for treating cancer for decades
- First- and second-generation camptothecins were highly potent but came with many liabilities like:
  - Bone marrow suppression (e.g., neutropenia, thrombocytopenia, anemia).
  - Life-threatening diarrhea
  - Pulmonary inflammation
  - Sever stomatitis
- The approvals of Trodelvy® and ENHERTU® show that the potency of camptothecins can be enhanced with tumor-directed targeting

VIP236 A THIRD-GENERATION SOLUTION

- Pan-tumor targeted optimized camptothecin delivery to the tumor
- Linker designed to release in the tumor microenvironment
- Payload optimized to resist transporter-mediated resistance and prevent recirculation

LEADS TO IMPROVED SAFETY IN THE CLINIC

- **No severe diarrhea, stomatitis, or ILD observed in the clinic**
- **Improved safety profile allows for combination with other agents and longer time on treatment**

OPPORTUNITY IN INDICATIONS WITH HIGH UNMET MEDICAL NEED

- TNBC
- Gastric cancer
- Lung cancer
- Ovarian cancer

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Solving ADC Challenges With the VersAptx™ Platform

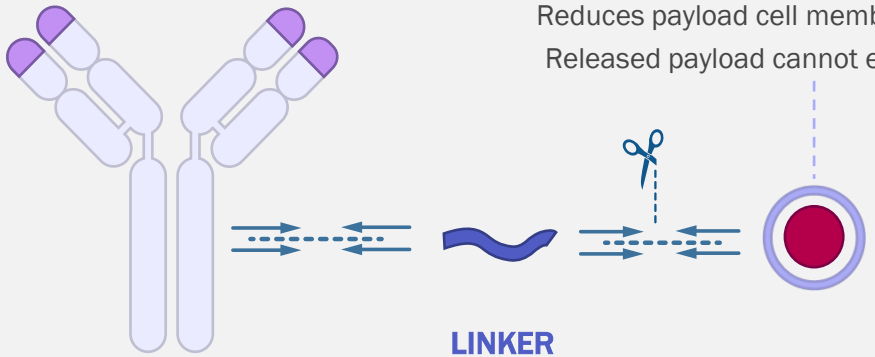
CLINICAL DATA VALIDATES NEXT-GENERATION ADC PLATFORM TECHNOLOGY

Known ADC Challenges

- Premature loss of cytotoxic payload
- Activity in healthy cells
- ADC aggregation and unspecific cellular uptake

LEADS TO
severe myelosuppression, infections, peripheral neuropathy, hepatotoxicity, and others

VersAptx™ PLATFORM



CELLTRAPPER®
Reduces payload cell membrane permeability
Released payload cannot enter healthy cells

LINKER
Exclusive intracellular cleavage by legumain, overexpressed in tumors

PAYLOAD
KSPi, a novel, high-potency payload with a MoA specific for dividing cells

Benefits

Legumain Linker
- Second level of tumor targeting via specific ADC activation

KSPi payload + Cell Trapper
- Potential for improved safety and tolerability
- Low/no toxicity in nondividing cells, no neurotoxicity
- Drug accumulation in target cells improves efficacy

Hydrophilic linker-payload
- Allows for high DAR without affecting PK
- No side effects associated with aggregation

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Phase 1 Dose-Escalation Study in Patients with CD123+ Relapsed/Refractory Hematologic Malignancies

VNC-943-101

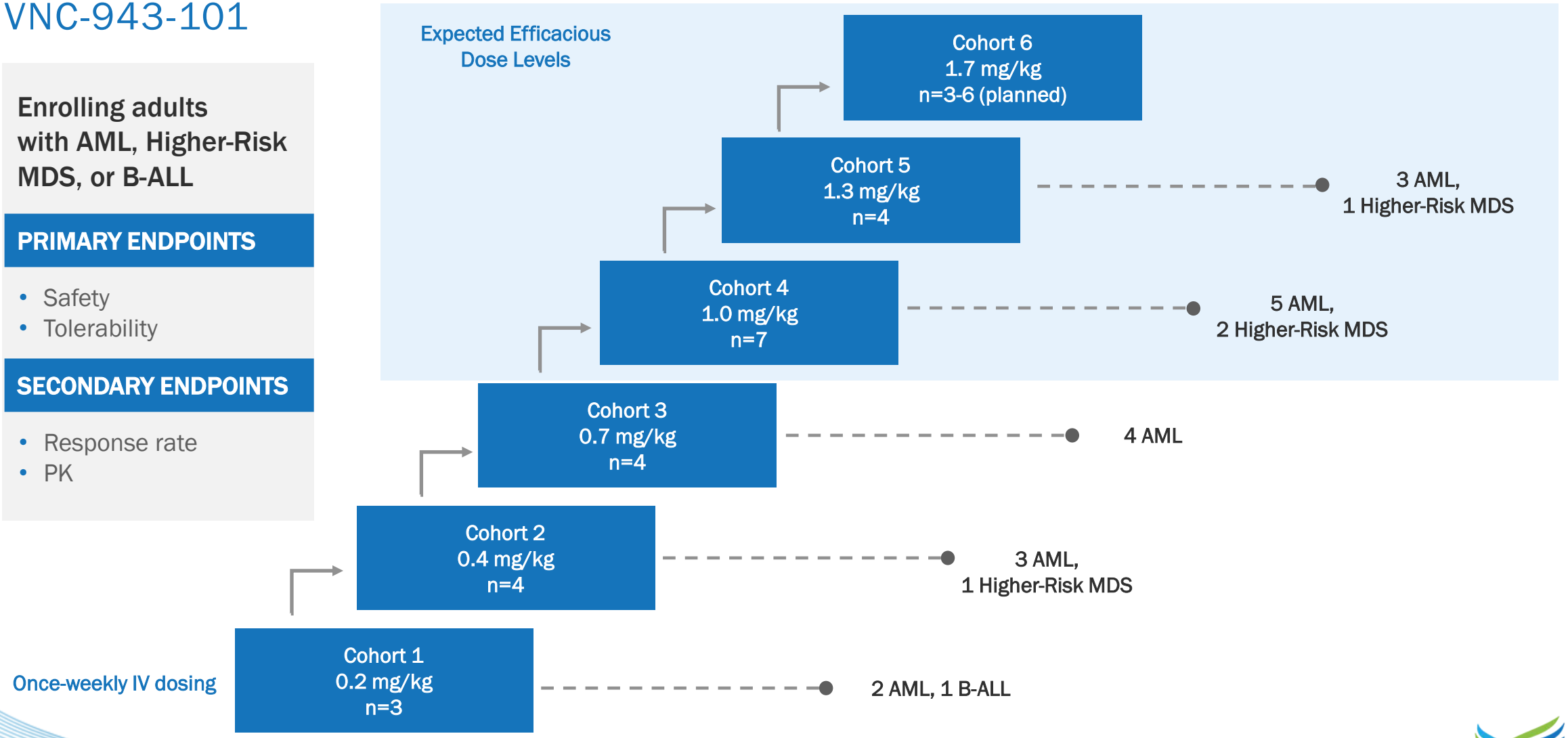
Enrolling adults with AML, Higher-Risk MDS, or B-ALL

PRIMARY ENDPOINTS

- Safety
- Tolerability

SECONDARY ENDPOINTS

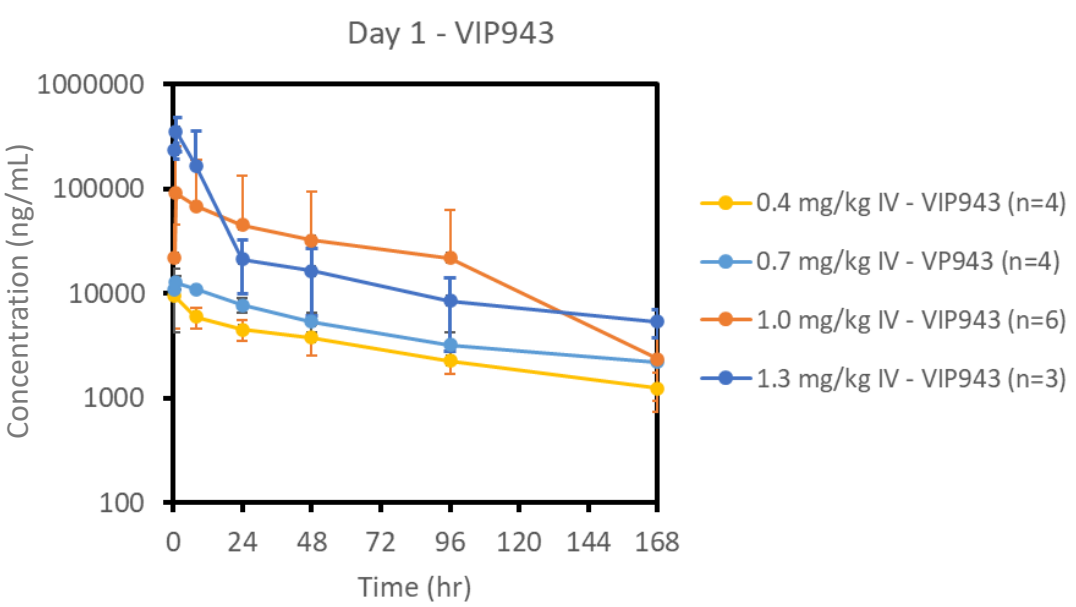
- Response rate
- PK

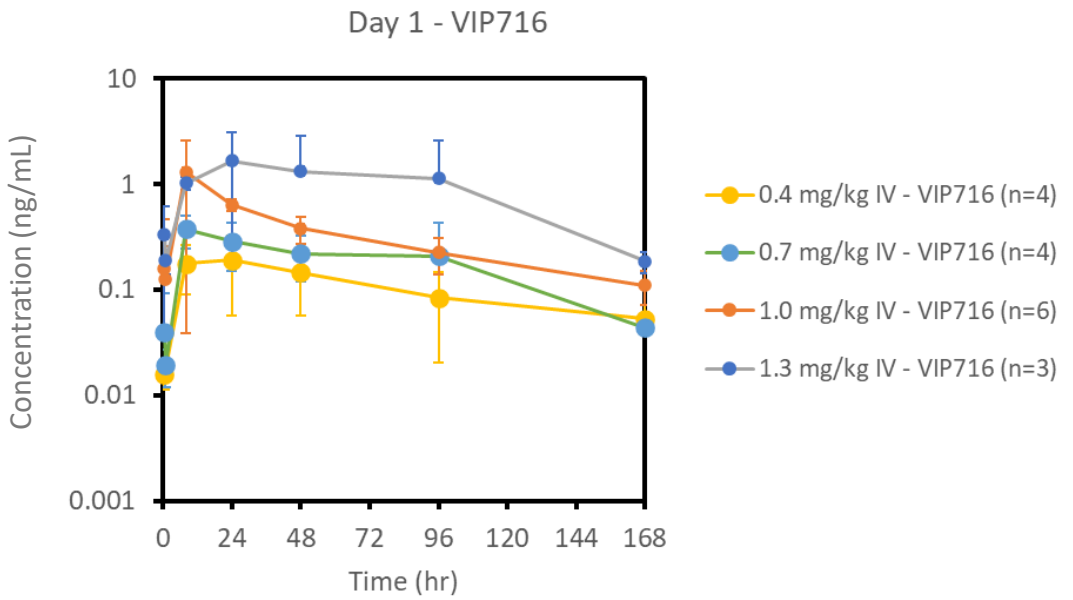


As of 29 Aug 2024
NCT06034275

Strong Legumain Linker Stability Confirmed by Low Levels of Circulating Payload

ON AVERAGE, ≤1% OF THE PAYLOAD FOUND IN THE PLASMA BETWEEN 0.4 TO 1.3 MG/KG





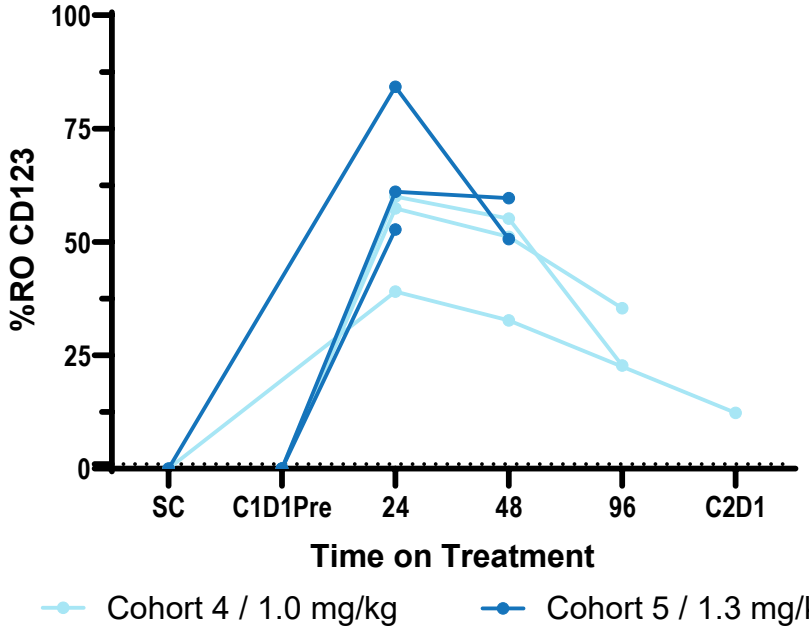
- Mean Metabolite:Parent (M:P) ratio of ≤1% on a molar basis indicating a stable linker
- Exposures of payload VIP716 are considered nontoxic (i.e. significantly below the IC50 values in cellular cytotoxicity assays)

Unaudited data. Subject to change.

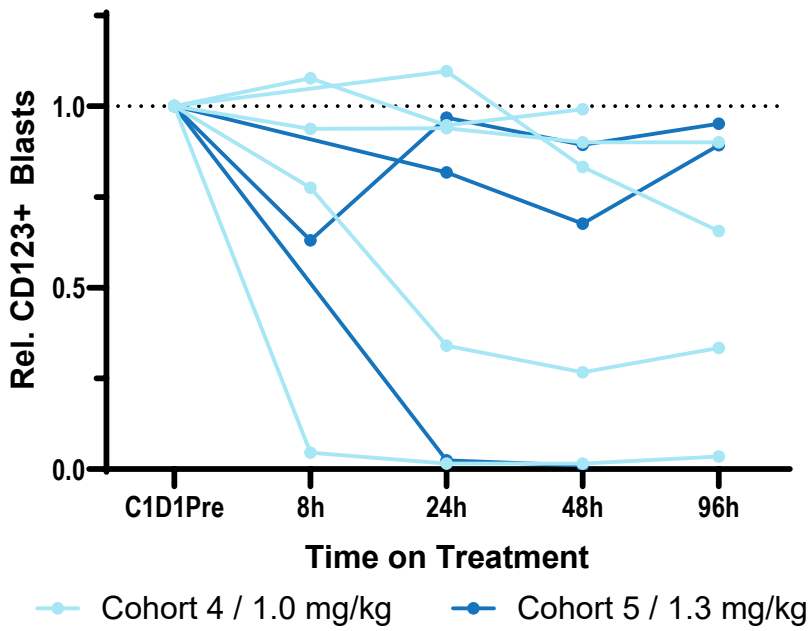
Elimination of CD123+ Blasts Validates ADC Cleavage and KSPi

REDUCTIONS SUSTAINED FOR 96 HOURS; TWICE WEEKLY DOSING COULD IMPROVE THERAPEUTIC BENEFIT

Receptor Occupancy for VIP943 during the Start of Cycle 1



Relative % of CD123+ Blasts During the Start of Cycle 1 of VIP943 Treatment



- Confirmed target engagement and selective internalization of the ADC
- Efficient ADC trafficking into the lysosome and linker cleavage by legumain
- KSP inhibition leads to apoptosis

Unaudited data. Subject to change.

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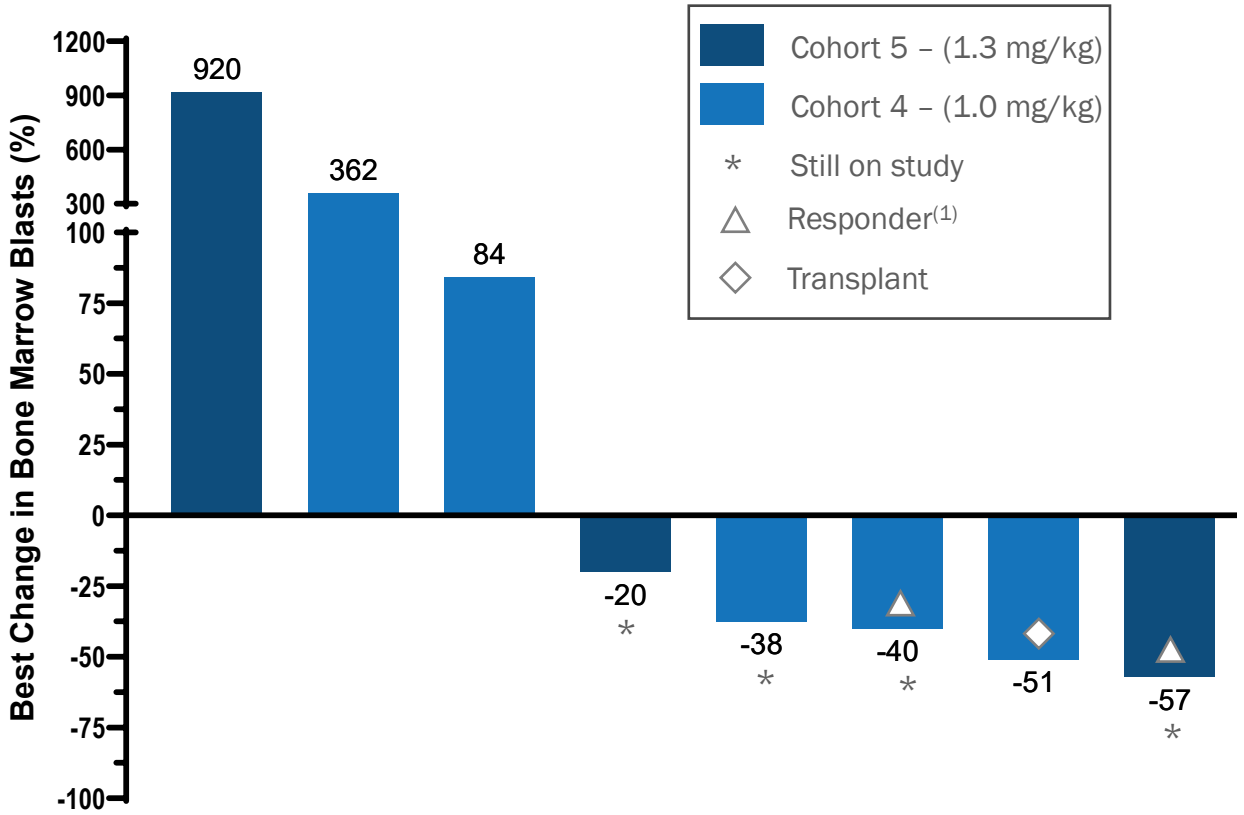
Bone Marrow Blast Reductions Evident at Efficacious Dose Levels

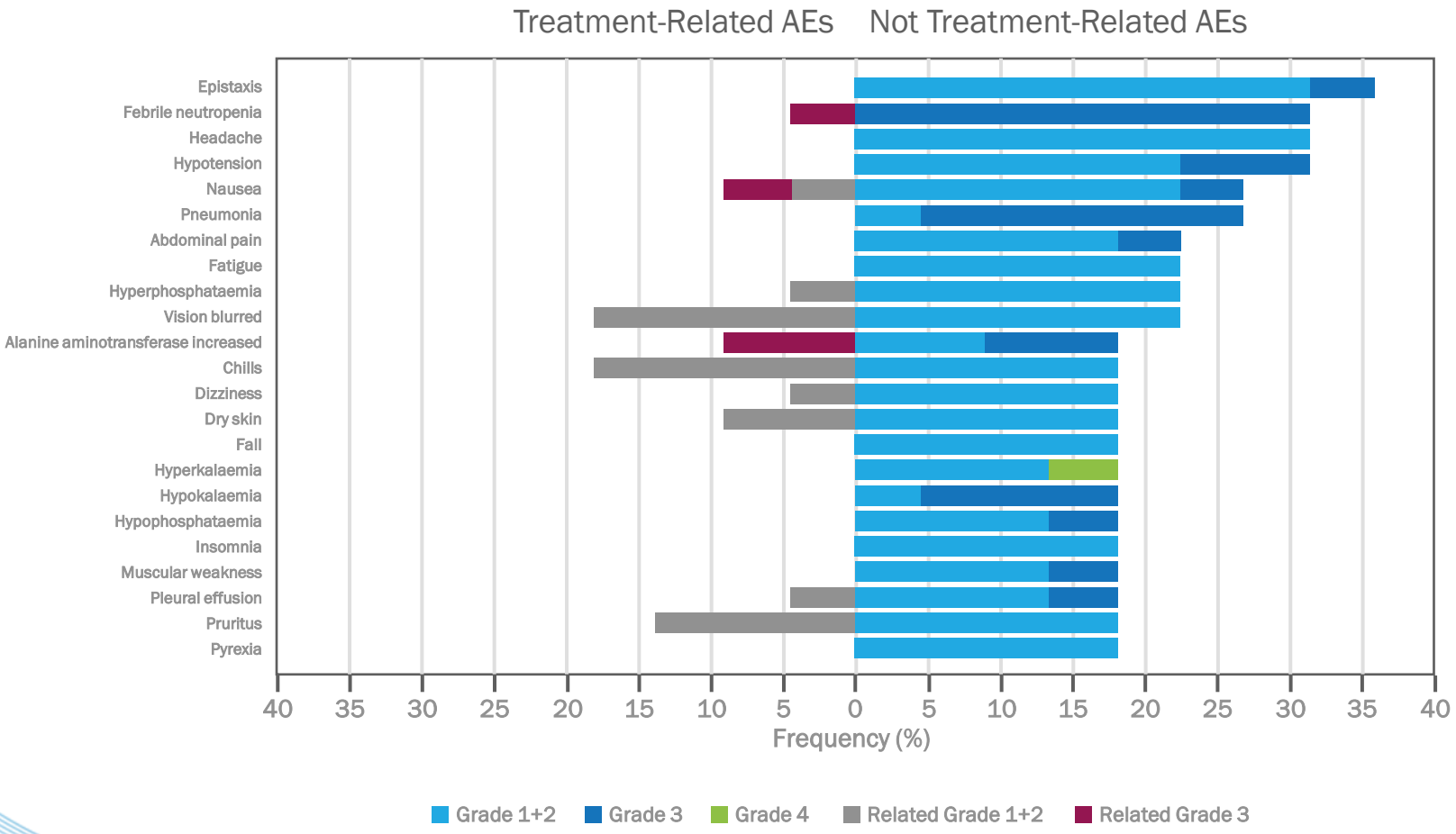


(1) De novo AML patient responder in cohort 4 is a CRi; refractory HR-MDS patient responder in cohort 5 is a CR_L

Unaudited data. Subject to change.

Demonstrated Safety in Phase 1 Dose Escalation Study

TREATMENT-EMERGENT ADVERSE EVENTS (>15%), ALL DOSE-LEVELS, N=22



VIP943 shows favorable safety and tolerability:

- No myelosuppression, cytokine release syndrome, interstitial lung disease, peripheral neuropathy, or veno-occlusive disease
- Grade 3-4 toxicities were generally manageable or reversible
- No dose-limiting toxicities to date

Data extract: 29AUG2024

Unaudited data. Subject to change.

Overview of Efficacy and Safety by Cohort

EARLY SIGNS OF DIFFERENTIATED THERAPEUTIC INDEX

	Dose Cohort				
	1 (0.2 mg/kg QW)	2 (0.4 mg/kg QW)	3 (0.7 mg/kg QW)	4 (1.0 mg/kg QW)	5 (1.3 mg/kg QW)
AML responses*	0/2	0/3	0/3	1/4 CRi	0/2
HR-MDS responses*	--	0/1	--	0/2	1/1 CR_L
B-ALL responses*	0/1	--	--	--	--
Transplant	0/3	0/4	1/3	1/6	0/3
DLTs	0/3	0/4	0/3	0/6	0/3
On study	0/3	0/4	0/3	2/6	2/3
Time on study (min, max months)	1.7-3.5	1.2-3.4	1.5-4.9	1.0-4.5+	1.0-3.0+

EMERGING SIGNS OF EFFICACY STARTING WITH COHORT 4 WITH NO INCREASE IN TOXICITIES

- No dose-limiting toxicities to date
- Patients remain on study in cohorts 4 and 5
- Dose escalation continues

CRi = complete remission with incomplete hematologic improvement; CR_L = complete remission with limited count recovery

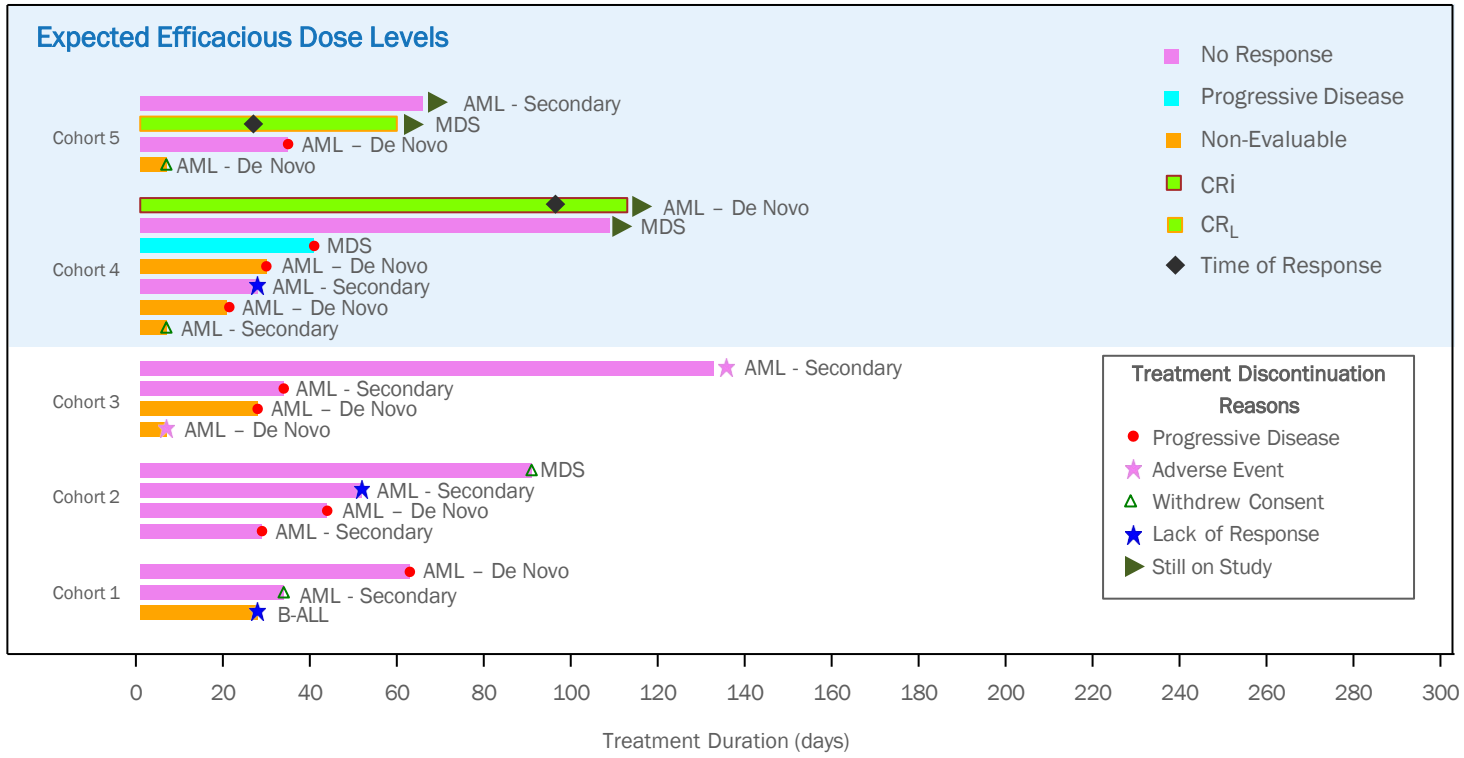
European LeukemiaNet (ELN) Criteria: https://doi.org/10.1182/blood.2022016867

International Working Group Criteria: https://doi.org/10.1182/blood.2022018604

*Patients with at least 3 doses of VIP943 or 1 on-treatment bone marrow assessment
QW = once weekly

Responses Achieved at Anticipated Efficacious Dose Levels

CRi and CR_L ACHIEVED AT ≥ 1.0 MG/KG DOSE LEVEL; FOUR PATIENTS REMAIN ON STUDY



- Per investigator assessment:
  - **One patient with AML has achieved CRi**
  - **One patient with HR-MDS has achieved CR_L**
- In cohorts 4 and 5, 44% of evaluable* patients (4 out of 9) remain on study

*1 AML patient in each dose level (n=2) withdrew consent after 1 dose of VIP943 and were not evaluable for response

Data extract: 29AUG2024; Unaudited data. Subject to change.

Promising Patient Responses Observed in HR-MDS and Relapsed AML

NOTABLE BLAST REDUCTION AND CLINICAL IMPROVEMENT IN EARLY CYCLES OF TREATMENT

74-year-old man with relapsed de novo AML	
Prior SOC included allogeneic stem cell transplant *On study since 09MAY*	
VIP943 at 1.0 mg/kg (Cohort 4)	**Response** • CRi on Cycle 4 Day 1 • Bone marrow blast <5% • ANC >1.0 x 10^9/L • Substantial reduction in CD123+ blasts to 20% observed 48 h after 1st dose
Patient remains on study.	

48-year-old woman with refractory HR-MDS and high IPSS-R (>4.5-6)	
Refractory to decitabine therapy *On study since 01JUL*	
VIP943 at 1.3 mg/kg (Cohort 5)	**Response** • CR_L on Cycle 2 Day 1 • Bone marrow blast <5% • Hematologic parameters stable • Potential candidate for subsequent allogeneic stem cell transplant
Patient remains on study.	

Additional Encouraging Results

CLINICAL IMPROVEMENT IN CHALLENGING CASES, WITH PATIENTS STILL ON STUDY

Bone marrow results showed trend toward improvement at Cycle 4 Day 1

VIP943 at 1.0 mg/kg (Cohort 4)

Background
- 76-year-old man with refractory HR-MDS and very high IPSS-R (>6)
- *Refractory to azacitidine treatment*

Primary Results
- At Cycle 4, Day 1, **bone marrow blasts were reduced by 37.5%,** bringing blast count down to 10% with an improvement to normocellular marrow

Patient planning for hospice elected to stay on study after discussing results with treating physician.

Bone marrow blast reduction after 1 cycle of treatment with VIP943

VIP943 at 1.3 mg/kg (Cohort 5)

Background
- 52-year-old man with refractory secondary AML with TP53 mutation
- Refractory to 6 different chemotherapies including venetoclax

Primary Results
- **20% reduction in bone marrow blast after one cycle** of treatment, bringing blast count down to 24%

Subject's experience of blurry vision with VIP943 has reversed and patient continues treatment as he believes VIP943 is making him feel better.

VIP943 treatment allowed for subsequent allogeneic stem cell transplant

VIP943 at 0.7 mg/kg (Cohort 3)

Background
- 62-year-old woman with MDS that transformed to AML
- AML refractory to azacitidine + venetoclax (2 cycles)

Outcome
- Ineligible for transplant during treatment with aza+ven due to poor performance status (nausea, vomiting, weight loss)
- Received 5 cycles of VIP943
- 2 episodes of blurry vision were managed and resolved
- Patient performance significantly improved allowing for transplant

Patient is off study. She has received FLAG-IDA-ven without issue and will be admitted soon for allogeneic transplant.

TP53 mutated AML represents an unmet medical need in AML and is a potential AA pathway.

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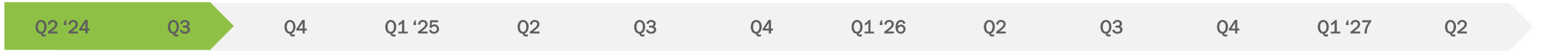
VIP943 Clinical Development Plan

PIPELINE WITHIN A MOLECULE



VIP943 PHASE 1 DOSE ESCALATION

- Patients with AML, higher-risk MDS, and B-ALL, currently ongoing
- Continue dose escalation and test twice-weekly dosing until we reach a biologically active dose
- Anticipated study conclusion: Q1 2025

VIP943 PHASE 1b DOSE OPTIMIZATION

- Per Project Optimus, dose optimization is part of the Phase 1 protocol
- Choose two or more doses, based on data from dose escalation study and continue monotherapy study
- Anticipated timing: Q3 2025 – Q1 2026

VIP943 DOSE EXPANSION

VIP943 R/R AML, INCLUDING MUTATED TP53

- Monotherapy and in combination with VEN + AZA
- Anticipated timing: Q2 2026 – Q2 2027

VIP943 FRONTLINE AML, INCLUDING MUTATED TP53

- Anticipated timing: Q2 2026 – Q4 2026

VIP943 HIGH-RISK MDS

- Anticipated timing: Q2 2026 – Q3 2026

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Discussion

M. Yair Levy, MD
Texas Oncology

Ahmed Hamdy, MD
Chief Executive Officer, Vincerx Pharma, Inc.

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Q&A

WE ASPIRE TO CONQUER CANCER

by addressing the unmet medical needs of patients with paradigm-shifting therapeutics.

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