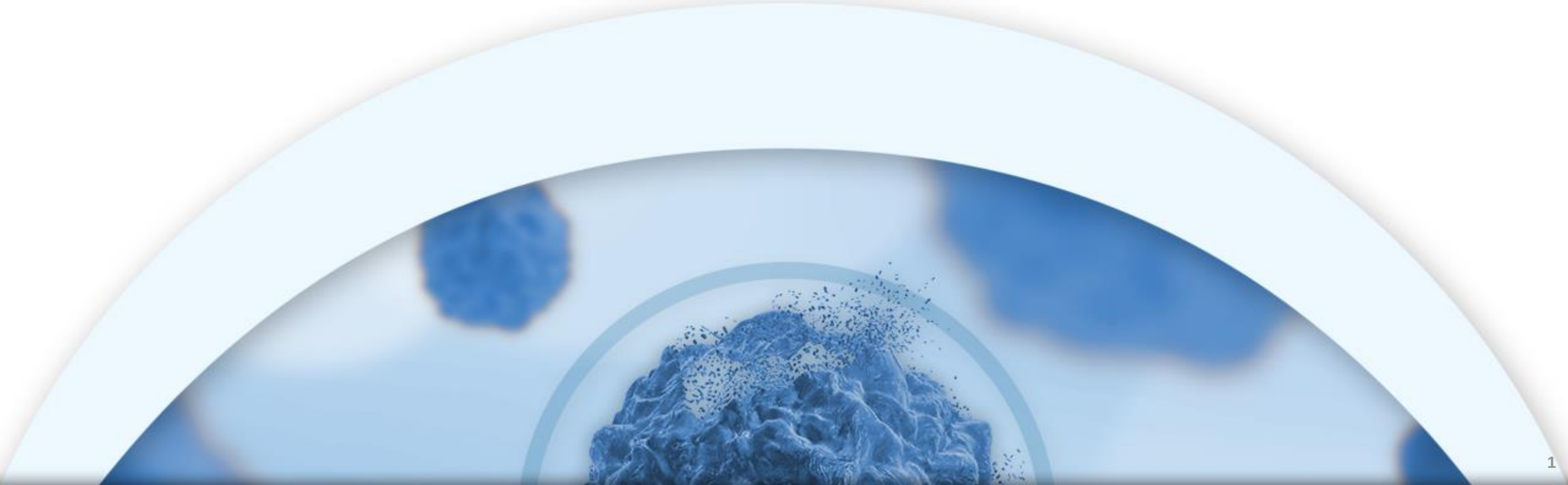
Key Opinion Leader (KOL) Call

June 11, 2021



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This presentation contains certain forward-looking statements about Curis, Inc. (“we,” “us,” or the “Company”) within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. Words such as “expect(s),” “believe(s),” “will,” “may,” “anticipate(s),” “focus(es),” “plans,” “mission,” “strategy,” “potential,” “estimate(s)”, "intend," "project," "seek," "should," "would" and similar expressions are intended to identify forward-looking statements. Forward-looking statements are statements that are not historical facts, reflect management’s expectations as of the date of this presentation, and involve important risks and uncertainties. Forward-looking statements herein include, but are not limited to, expectations of the potential for the Company’s proprietary drug candidate CA-4948, including with respect to the potency, anti-cancer activity, durability and tolerability of CA-4948, future studies with respect to CA-4948, the potential advantages and benefits of CA-4948 and small molecule checkpoint antagonists, and the Company’s plans to advance its development programs. These forward-looking statements are based on our current expectations and may differ materially from actual results due to a variety of important factors including, without limitation, risks relating to: whether any of our drug candidates will advance further in the clinical development process and whether and when, if at all, they will receive approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies; whether historical preclinical results will be predictive of future clinical trial results; whether historical clinical trial results will be predictive of future trial results; whether any of our drug candidate discovery and development efforts will be successful; whether any of our drug candidates will be successfully marketed if approved; our ability to achieve the benefits contemplated by our collaboration agreements; management’s ability to successfully achieve its goals; the sufficiency of our cash resources; our ability to raise additional capital to fund our operations on terms acceptable to us or the use of proceeds of any offering of securities or other financing; general economic conditions; competition; and the other risk factors contained in our periodic and interim reports filed with the Securities and Exchange Commission which are available on the SEC website at www.sec.gov. You are cautioned not to place undue reliance on these forward-looking statements that speak only as of the date hereof, and we do not undertake any obligation to revise and disseminate forward-looking statements to reflect events or circumstances after the date hereof, or to reflect the occurrence of or non-occurrence of any events, except as required by law.

Introduction/Welcome

James Dentzer, President & CEO

Key Opinion Leader

Dr. Guillermo Garcia-Manero, UT MD Anderson Cancer Center

A PHASE 1, DOSE ESCALATION TRIAL WITH NOVEL ORAL IRAK4 INHIBITOR CA-4948 IN PATIENTS WITH ACUTE MYELOGENOUS LEUKEMIA OR MYELODYSPLASTIC SYNDROME – INTERIM REPORT

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June 11, 2021
Program Section: Novel Target in MDS
Abstract: S165

Disclosures

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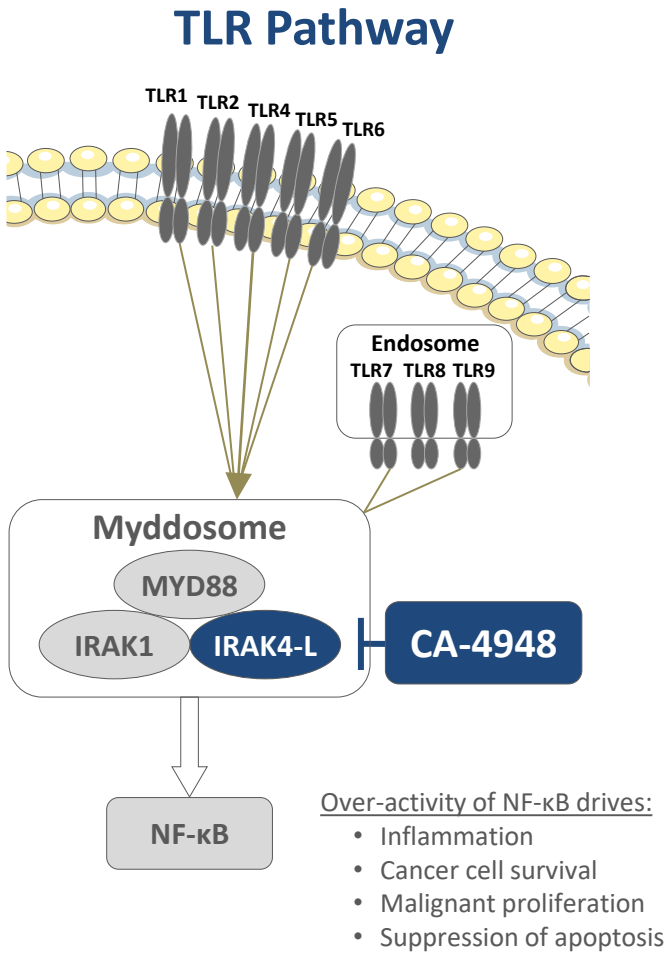
Introduction

- Interleukin-1 receptor associated kinase 4 (IRAK4) plays an essential role in toll-like receptor (TLR) and interleukin 1 receptor (IL-1R) signaling pathways
- These pathways are frequently dysregulated in Non-Hodgkin Lymphomas (NHL) and AML/MDS[1]
- Oncogenic IRAK4-L, frequently driven by spliceosome mutations, is preferentially expressed in > 50% of AML/MDS patients[2,3]
- Activated IRAK4 has been identified as a driver of adaptive resistance in AML[4]

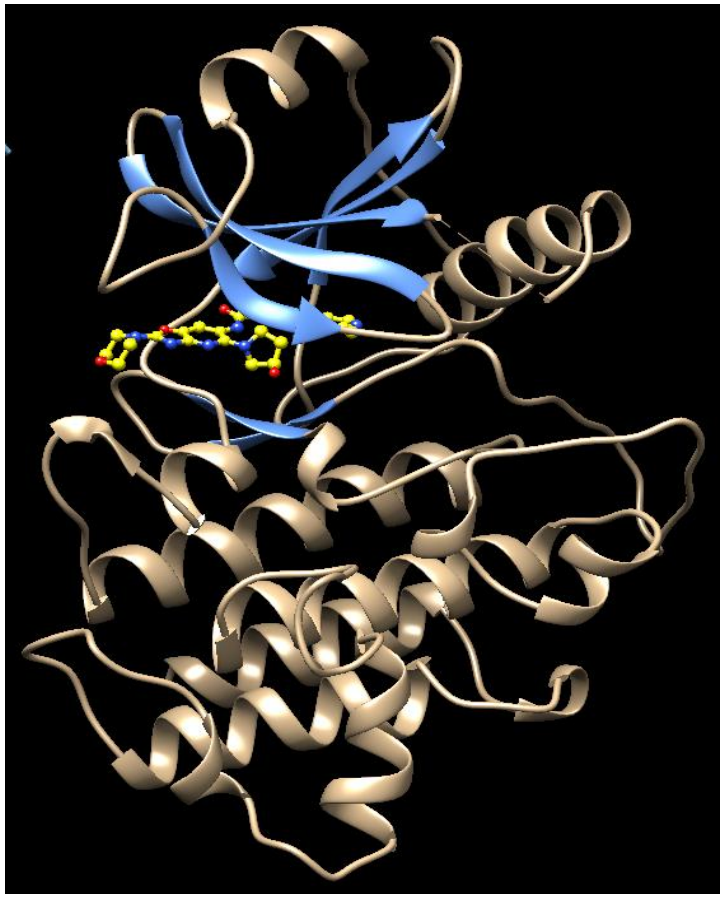


1) Rhyasen GW and Starczynowski DT. Br J Cancer 2015
2) Choudhary G *et al.* Blood 2019
3) Smith MA *et al*. Nat Cell Biol 2019
4) Melgar K *et al.* Sci Transl Med 2019

CA-4948 is a novel, small molecule, IRAK4 inhibitor

- First-in-class IRAK4 inhibitor in oncology
- Inhibits hematological malignancies that are driven by over-activity of the TLR/IL-1R pathway, which is dependent on IRAK4
- CA-4948 also inhibits FLT3-mutated AML *in vitro* and *in vivo*
- High binding affinity to IRAK4 (23 nM) and FLT3 (31 nM)
- No myelosuppressive DLTs
- Excellent oral bioavailability
- Dose-dependent PK with clear PD correlates
- Safe (RP2D 300 mg BID) and active in relapsed or refractory (R/R) NHL

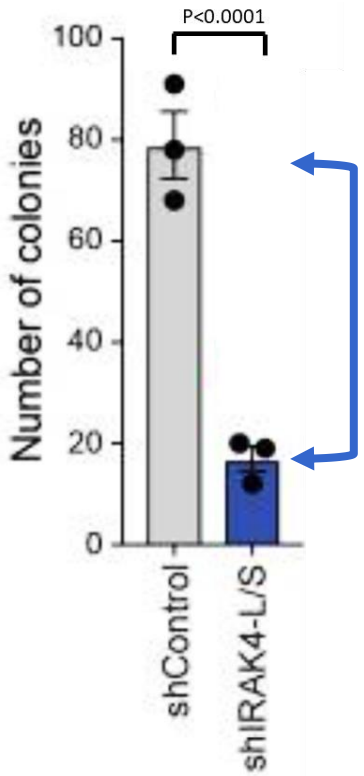
IRAK4/CA-4948 Co-crystal Structure



ATP-competitive, type 1 reversible inhibitor

CA-4948 targets IRAK4-L, a key driver of leukemia

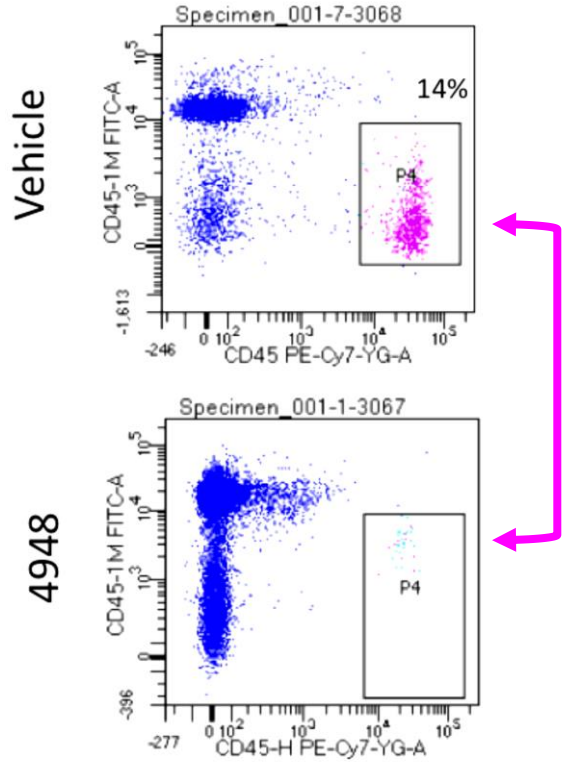
IRAK4-L is oncogenic



*Blocking IRAK4-L reduces formation of **leukemia colonies** in preclinical studies*[1]

IRAK4-L knockdown models demonstrate genetic link to oncogenic immune signaling in AML/MDS[1]

CA-4948 targets IRAK4-L



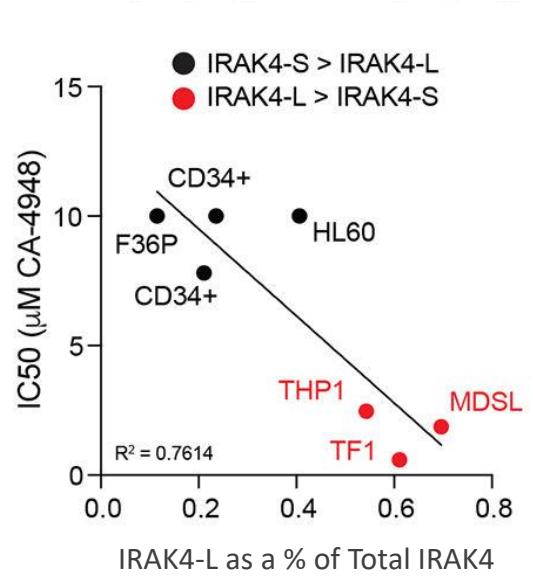
*CA-4948 treatment reduces **leukemic blasts** in patient-derived xenografts*[2]

In preclinical model, IRAK4-L inhibition with CA-4948 demonstrates anti-cancer activity consistent with knockdown models[2]

1) Smith et al. Nat Cell Biol 2019
2) Choudhary et al. AACR 2017

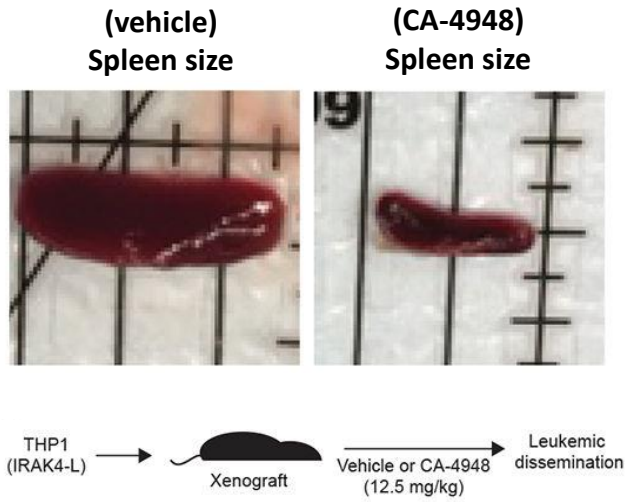
CA-4948 reduces tumor burden in preclinical models

CA-4948 is more active in cell lines overexpressing IRAK4-L



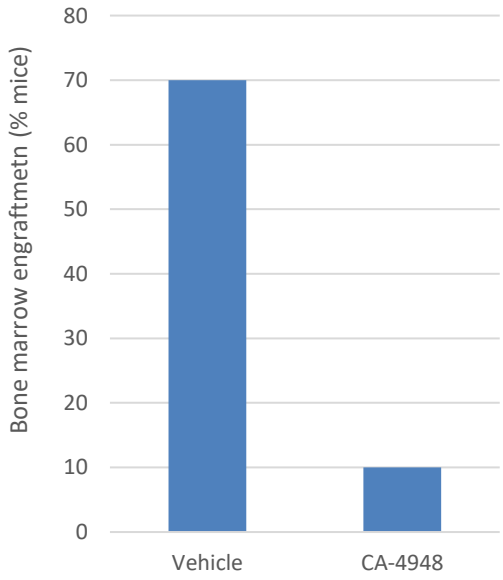
Smith et al. 2019

Xenografts treated with CA-4948 maintained normal spleen size (surrogate for leukemic burden)



Smith et al. 2019

Treatment with CA-4948 prevented leukemic engraftment in almost all xenografts

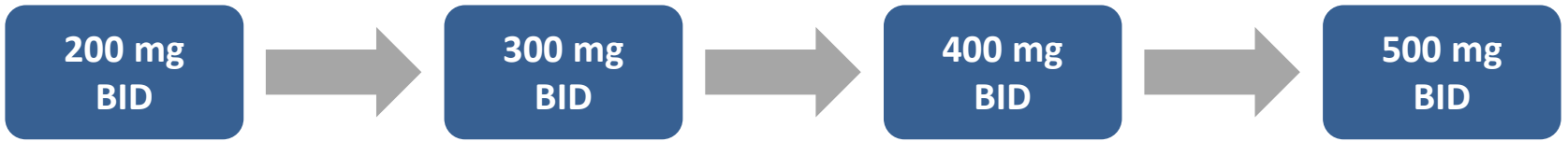


Smith et al. 2019

IRAK4-L is a negative prognosticator of survival

Clinical study design

Multicenter, single arm, Phase 1 dose escalation study of CA-4948 monotherapy in adult patients with AML or high risk MDS; treated in continuous 28-day cycles in the absence of unacceptable toxicity or disease progression (NCT04278768)



Primary Objective

Safety and RP2D

Secondary Objectives

Pharmacokinetics

Initial efficacy, including ORR for evaluable patients with baseline and at least 1 follow-up assessment

Exploratory Objectives

Pharmacodynamics

Biomarkers related to mechanism of action

Patient eligibility

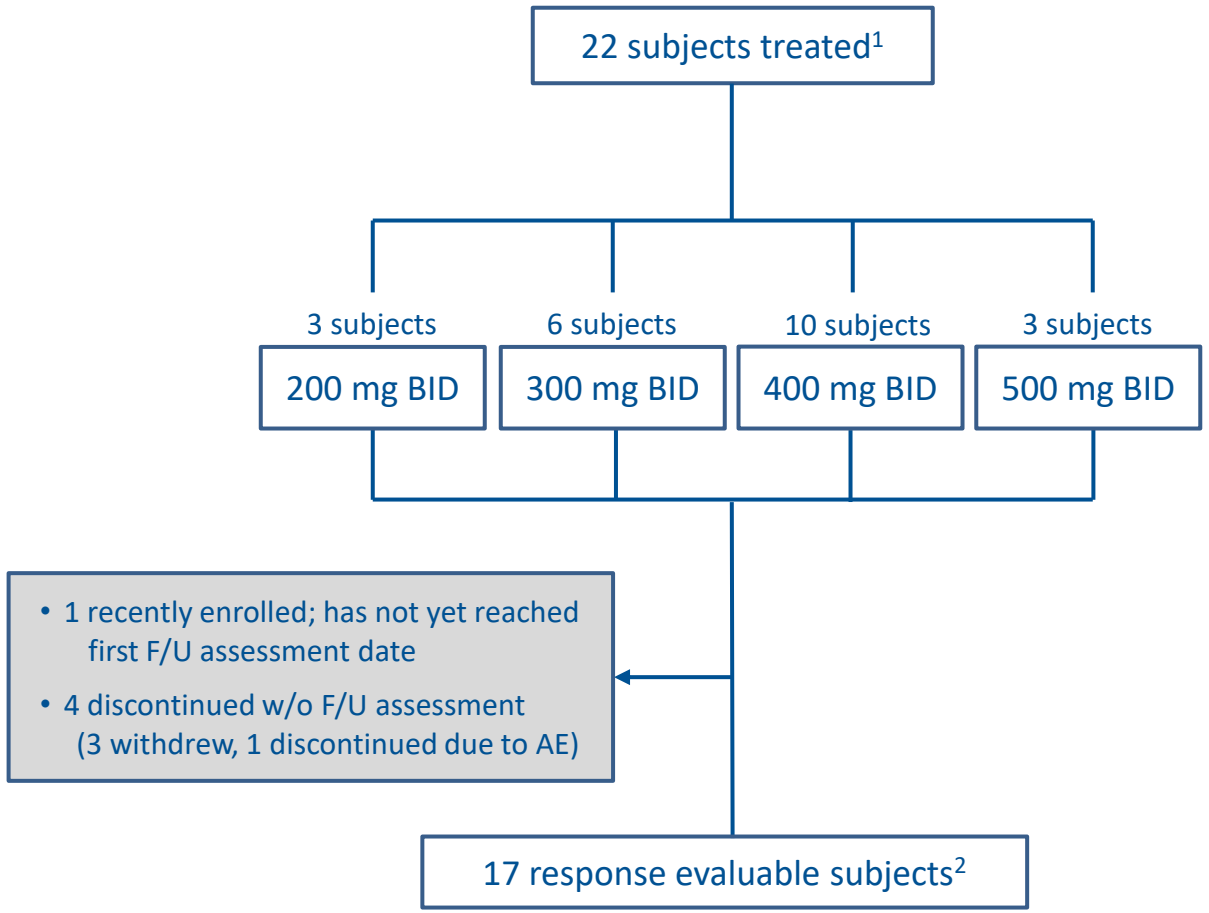
Inclusion:

- hrMDS or AML (WHO 2016 classification)
- ≥ 18 years of age
- ECOG ≤ 2
- R/R after failing at least 1 standard treatment

Exclusion:

- Acute promyelocytic leukemia (APL, M3)
- Active central nervous system leukemia
- Blast stage of chronic myelogenous leukemia
- Allo-HSCT within 60 days of the first dose of CA-4948 or clinically significant GvHD

Baseline characteristics



Characteristics		Patients (n=22)
Female n (%) : Male n (%)		5 (23) : 17 (77)
Age (yrs): median (range)		74 (32-87)
Race, n (%)	White	18 (82)
	African American	1 (4)
	Not reported	3 (14)
ECOG: n 0/1/2		7/11/4
Diagnosis	AML, n (%)	11 (50)
	hrMDS, n (%)	11 (50)
Median platelets (10^3/mm^3) (range)		33 (7, 275)
Median ANC (10^3/mm^3) (range)		1.2 (0.1, 14.8)
Median lines of prior therapy (range)		2 (1-4)
Prior therapy, n (%)	Azacitidine	14 (64)
	Decitabine	7 (32)
	Cytarabine	3 (14)
	Venetoclax	10 (45)
Cytogenetic risk, n (%)[3]	AML (favorable/intermediate/ adverse)	1 (10) / 2 (20) / 7 (70)
	hrMDS (good/intermediate/poor/ very poor)	1 (9) / 4 (36) / 3 (27) / 3 (27)
Relavant mutations[4]	FLT3	1
	SF3B1	2
	U2AF1	2

1) Data extraction date: Apr 30th, 2021
2) Response evaluable: all patients with both baseline and post-baseline assessments (or progressive disease before first follow-up assessment)
3) Analysis for cytogenetic risks includes 10 AML patients (ELN) and 11 hrMDS patients (IPSS-R)
4) Mutational analysis is ongoing

Treatment-related adverse events occurring in ≥ 2 patients

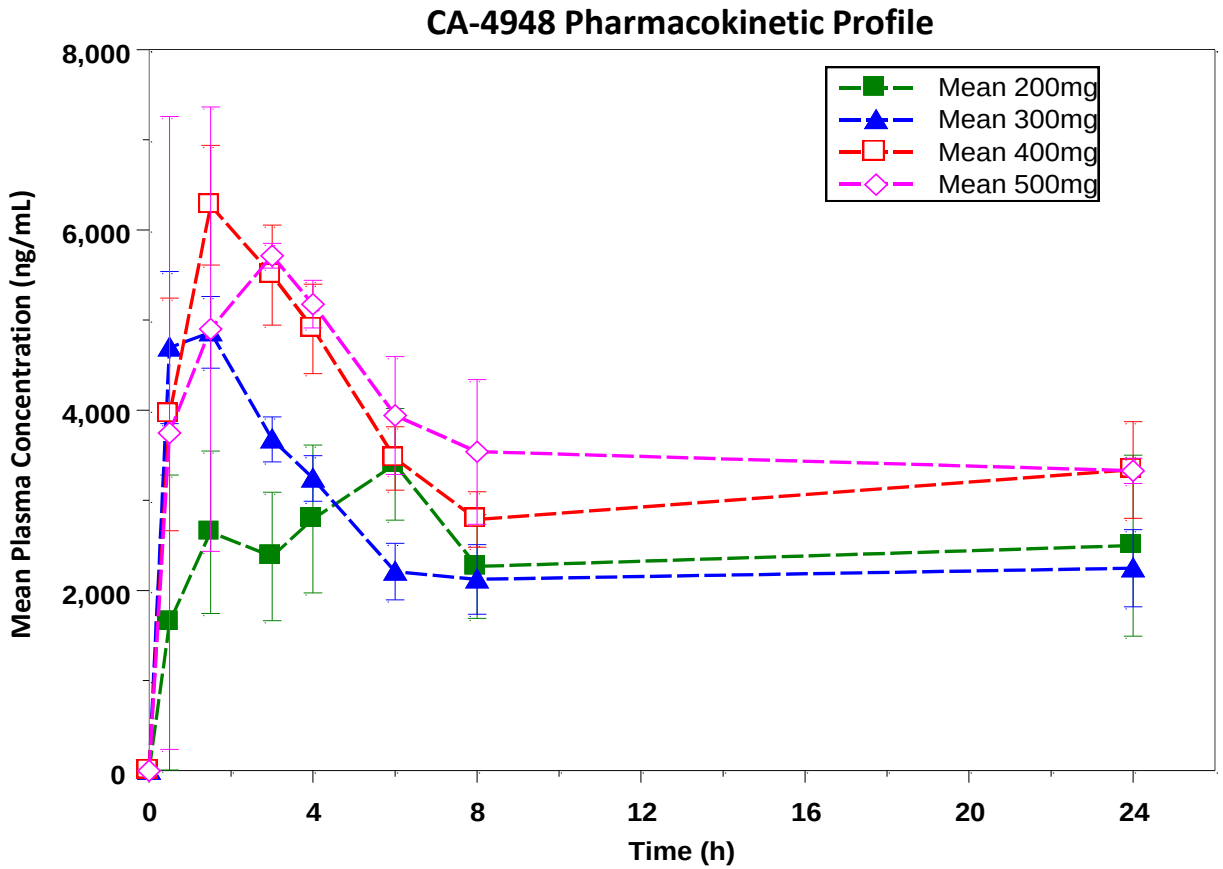
Per patient, highest grade

Preferred Terms	200 mg BID (n=3) Grade All	200 mg BID (n=3) Grade 3 or 4	300 mg BID (n=6) Grade All	300 mg BID (n=6) Grade 3 or 4	400 mg BID (n=10) Grade All	400 mg BID (n=10) Grade 3 or 4	500 mg BID (n=3) Grade All	500 mg BID (n=3) Grade 3 or 4	All (n=22) All Grades n (%)	All (n=22) Grade 3 or 4 n (%)
Dizziness	2	1	0	0	1	0	2	0	5 (22.7)	1 (4.5)
Nausea	1	0	1	0	0	0	2	0	4 (18.2)	0
Alanine aminotransferase increased	1	1	1	0	0	0	1	0	3 (13.6)	1 (4.5)
Fatigue	0	0	1	0	0	0	2	0	3 (13.6)	0
Muscular weakness	0	0	1	0	2	0	0	0	3 (13.6)	0
Myalgia	0	0	0	0	2	0	1	0	3 (13.6)	0
Chromaturia	0	0	0	0	2	0	0	0	2 (9.1)	0
Diarrhoea	0	0	1	0	1	0	0	0	2 (9.1)	0
Dyspnoea	0	0	1	0	1	0	0	0	2 (9.1)	0
Presyncope	0	0	1	0	1	1	0	0	2 (9.1)	1 (4.5)
Rhabdomyolysis	0	0	0	0	0	0	2	1	2 (9.1)	1 (4.5)

- No DLTs was observed for 200-400 mg BID cohorts during the dose-escalation phase
- DLTs observed in 2 patients at 500 mg BID (1 patient with Gr 3 rhabdomyolysis and 1 patient with Gr 3 syncope), both AEs resolved after dosing interruption; rhabdomyolysis AE was quickly detected by elevated CPK, did not involve renal dysfunction, and was quickly resolved after dosing interruption

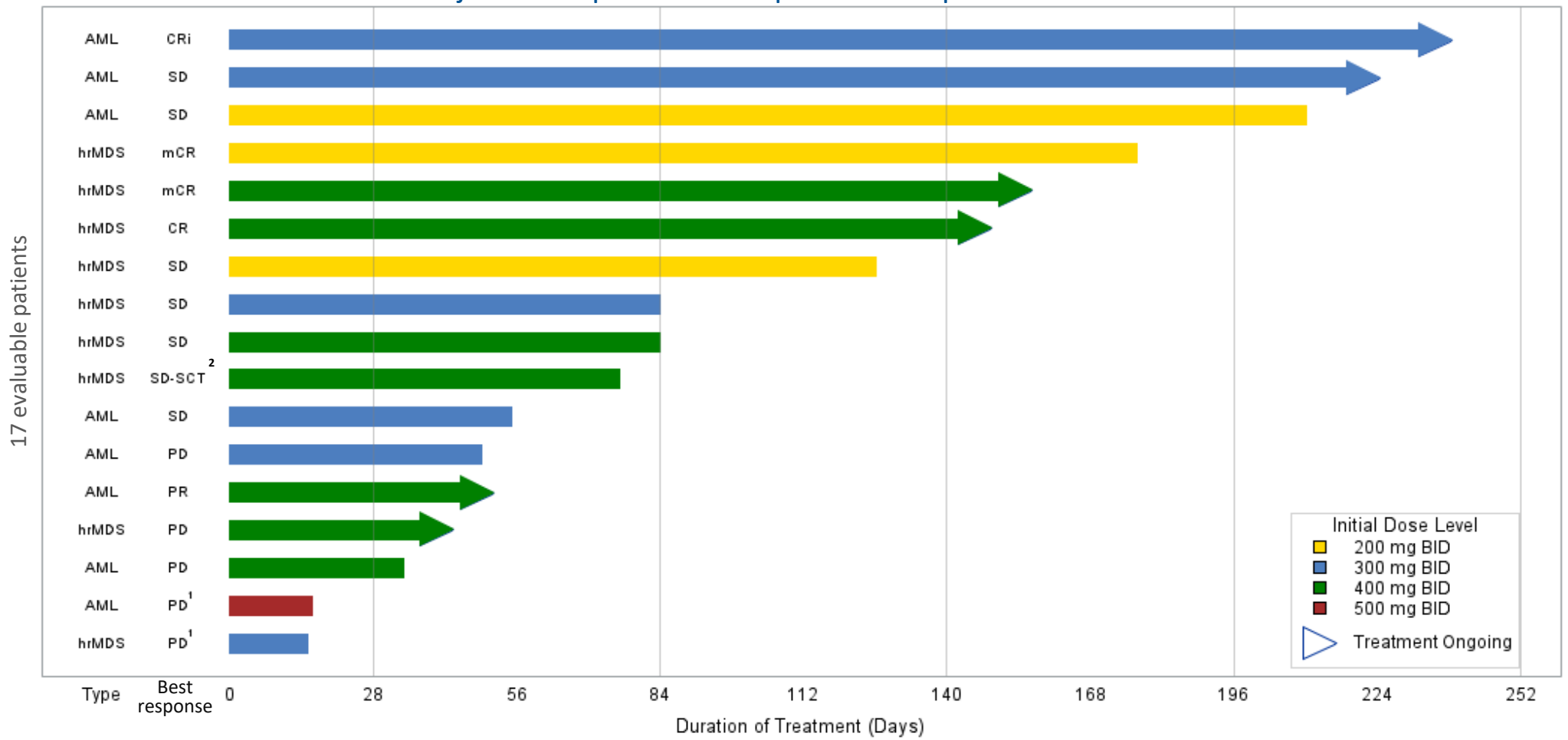
Predictable PK observed

- Half-life ~6 hours
- Rapidly absorbed with maximum plasma concentrations observed at 0.5-3.0 hours post dose
- CA-4948 exposure levels not altered in the presence of strong CYP450 inhibitors (*e.g.*, anti-fungal azoles)
- Dose proportional exposure with minimal or no accumulation with continuous BID administration



Treatment duration and patient response

5 objective responses and 1 patient who proceeded to SCT



Best Response

hrMDS (n=9)

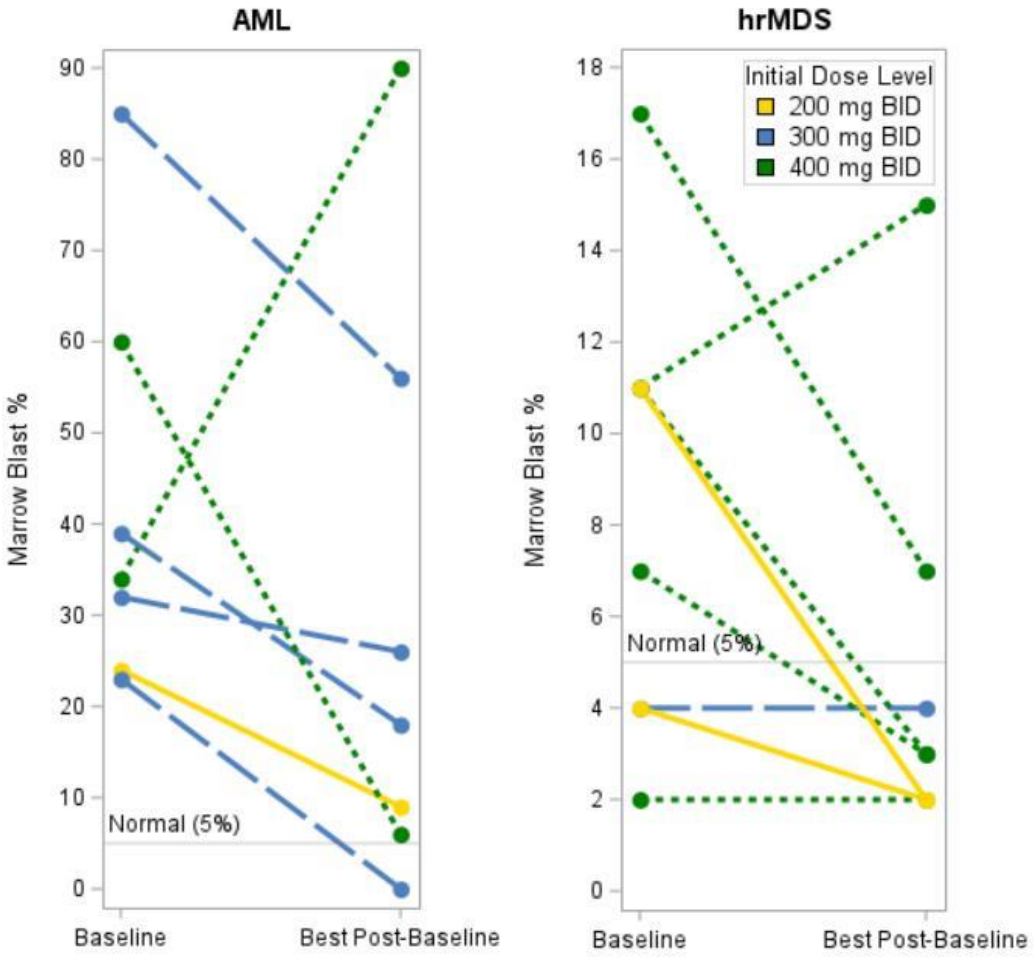
CR	1
mCR	2
SD	4
PD[1]	2

AML (n=8)

CRi	1
PR	1
SD	3
PD[1]	3

1) Two patients discontinued treatment due to PD prior to first follow-up disease assessment
2) One patient who achieved SD was able to proceed to stem cell transplant (SCT)

Reduction of marrow blasts achieved in 10 of 12 patients with elevated blast counts at baseline



Dose level	Diagnosis	Baseline blast (%)	Post-tx blast (%)	Change
200 mg BID	hrMDS	11	2	-82%
	AML	24	9	-63%
	hrMDS	4	2	-50%
300 mg BID	hrMDS	4	4	0%
	AML	23	0	-100%
	AML	39	18	-54%
	AML	32	26	-19%
	AML	85	56	-34%
	hrMDS	11	n/a	n/a
400 mg BID	AML	60	6	-90%
	hrMDS	17	7	-59%
	hrMDS	7	3	-57%
	hrMDS	2	2	0%
	hrMDS	11	15	36%
	hrMDS	11	3	-73%
	AML	34	90	165%
500 mg BID	AML	28	n/a	n/a

17 evaluable patients: 12 patients had elevated blasts at baseline
3 patients had marrow blasts <5% at baseline (in the normal range)
2 patients discontinued treatment due to PD prior to first disease assessment

Durable responses achieved in a high-risk population

- Responses achieved in heavily pre-treated, late-line patient population
- Responses achieved in spliceosome and FLT3 mutated patients supports CA-4948 dual mechanism of action
- FLT3 patient had 90% blast reduction at C2D1 (from 60% to 6%)

Dx	Cytogenetics (ELN, IPSS-R[3])	Molecular Mutations	Prior Therapies		CA-4948 Duration (months)	Best Response to CA-4948
			# Lines	Therapy		
t-hrMDS[1]	Intermediate	ASXL1, NF1, PHF6, **U2AF1**	1	azacitidine	6	Marrow CR
sAML[2]	Favorable	RUNX1, WT1, **SF3B1**	1	decitabine	8	CRi MRD-
AML	Intermediate	CBLC, DNMT3A, SMC1A, IDH2, STAG2, ETV6	4	cytarabine/daunorubicin cytarabine/idarubicin cytarabine/mitoxantrone high-dose cytarabine	7	SD
hrMDS	Intermediate	CEP8	1	decitabine	5	CR
hrMDS	Poor	RUNX1, NFE2, **SF3B1**	2	guadecitabine lenalidomide	5	Marrow CR
sAML[2]	Adverse	ASXL1, CSF3R	3	azacitadine lenalidomide cytarabine/daunorubicin	7	SD
AML	Adverse	**FLT3**, ASXL1, BCOR, CEBPA, CSF3R, EZH2, NRAS, RUNX1, STAG2, TET2	2	decitabine/venetoclax gilteritinib	2	PR

1) Therapy-related hrMDS
2) Secondary AML
3) ELN scoring for AML; IPSS-R scoring for hrMDS

Signs of hematologic improvement observed in patients achieving significant marrow blast reduction

- Following reduction in marrow blasts, patients saw signs of hematologic recovery
- Full hematologic recovery may be delayed or prevented by damage to the marrow from both disease and prior lines of cytotoxic therapy
- Patients who have not seen marrow blast reduction return to normal range have experienced limited or no hematologic recovery

mCR
82% blast reduction (11 to 2)
1 prior line of therapy

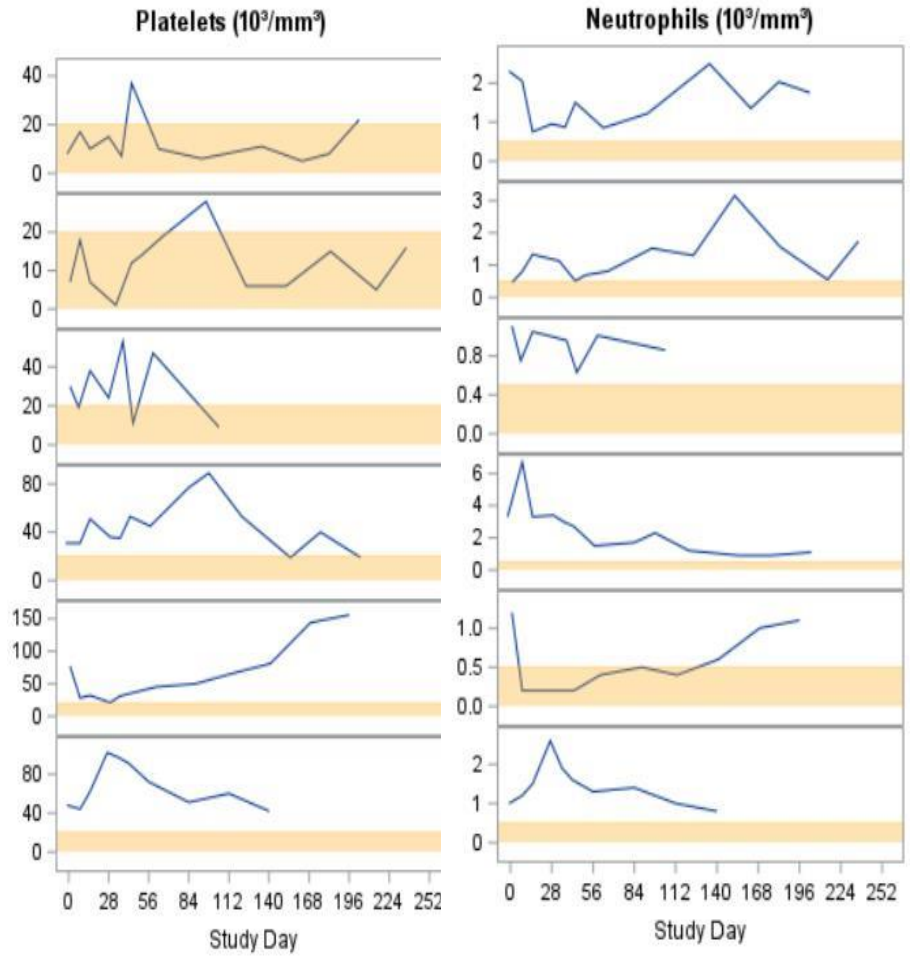
SD
63% blast reduction (24 to 9)
3 prior lines of therapy

mCR
57% blast reduction (7 to 3)
2 prior lines of therapy

CRi, MRD-
100% blast reduction (23 to 0)
1 prior line of therapy

SD
54% blast reduction (39 to 18)
4 prior lines of therapy

CR
73% blast reduction (11 to 3)
1 prior line of therapy



Orange bands denote increased bleeding or infection risk : < $20x10^3/mm^3$ for platelets and < $0.5x10^3/mm^3$ for neutrophils.

Genomic analyses suggest disease-modifying activity

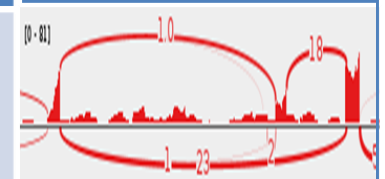
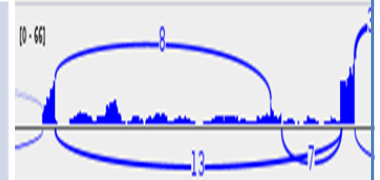
- Genomic analyses depicted are of samples from two patients
- DNA sequencing demonstrates the reduction of variant allele frequency after CA-4948 treatment
- RNA sequencing demonstrates the reduction of long/short ratio of IRAK4 after CA-4948 treatment

(NGS)

Patient DNA Sequencing

(RNA-seq)

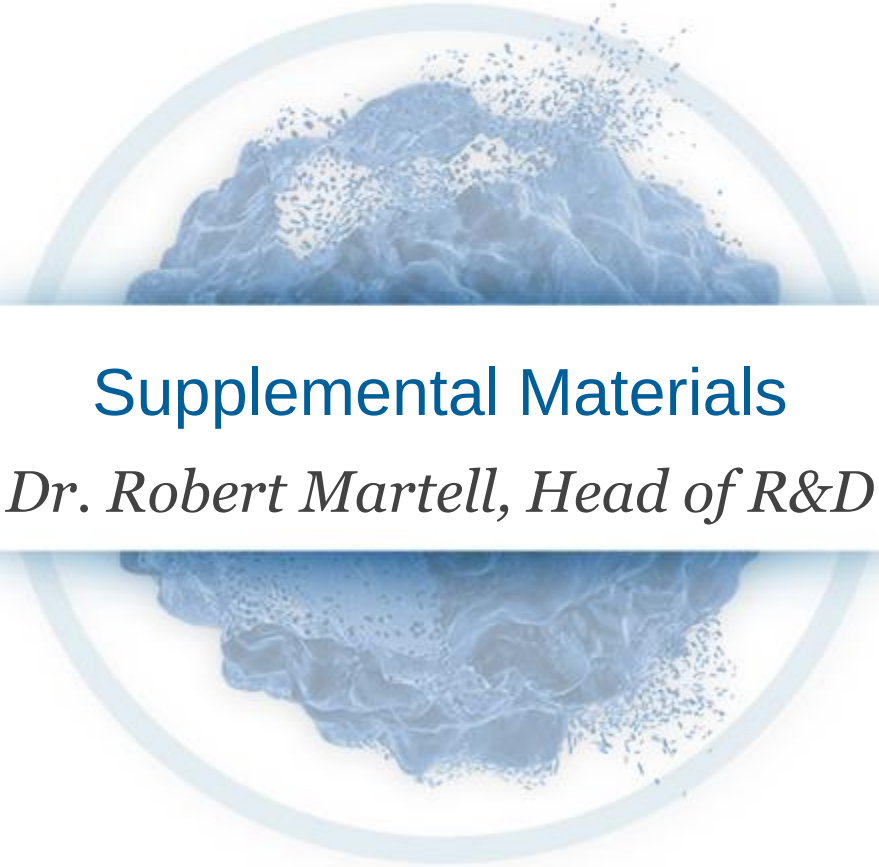
Patient RNA Sequencing

CA-4948 Tx Cycle	Long/Short Ratio	3 EXON 4 5
Control: Healthy CD34	18/23 (0.78)	
C2D1	8/7 (1.14)	
C4D1	7/13 (0.53)	

Summary

- Oral CA-4948 monotherapy is safe and well tolerated at 200, 300, and 400 mg BID
- Dose proportional exposure with minimal or no accumulation with continuous BID administration
- Clear anti-cancer activity in R/R AML and hrMDS patients:
  - 3 of 3 evaluable patients with IRAK4-related spliceosome mutations achieved a marrow CR or better
  - All patients with objective response also showed signs of hematologic recovery
- Next step in expansion:
  - Monotherapy in molecularly defined subgroups (spliceosome and FLT3 patient populations)
  - Combination therapy with azacitidine and venetoclax

Thank you to the participating trial investigators, clinical staff, the patients and their families



Supplemental Materials

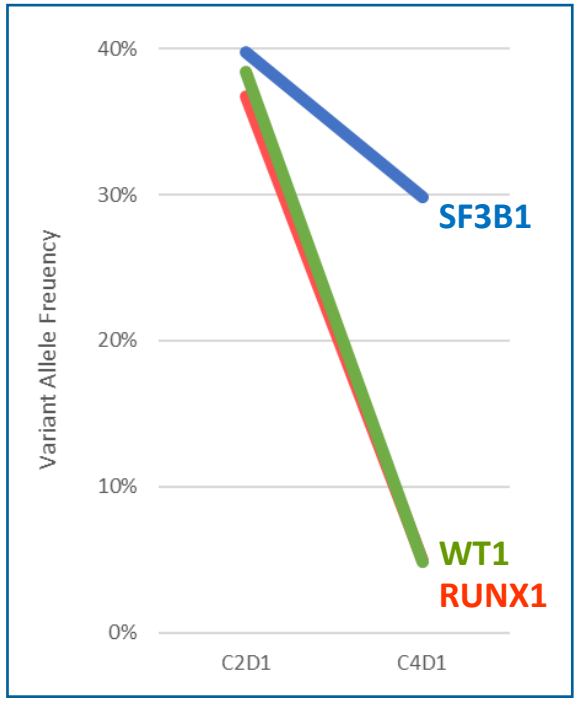
Dr. Robert Martell, Head of R&D

Patient Case Study #1

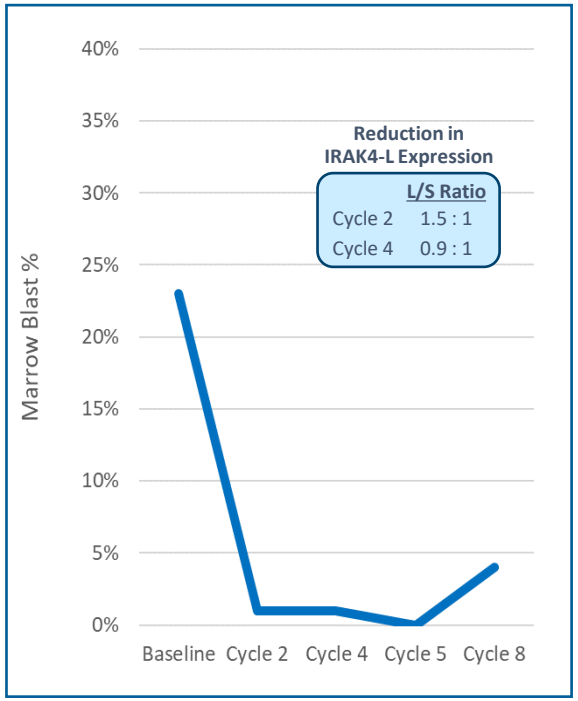
CA-4948 modifies disease in patient with spliceosome mutation

Disease	sAML	
Dose	300 mg BID	
ECOG Status	1	
Prior Lines of Therapy	1	decitabine
Known Mutations	**SF3B1**, RUNX1, WT1	
Cytogenetic Risk	ELN: Favorable	
Best Response	CRi, MRD-	

DNA Sequencing indicates disease modification



Marrow Blast Reduction deepened after several cycles



- Marrow CR reported at ASH 2020
- Response deepened to CRi by EHA 2021
- Decreases in cancer-associated mutations and IRAK4-L expression demonstrate CA-4948 is disease-modifying
- Supports rationale of expansion cohort in monotherapy for sub-population of patients with spliceosome mutation

Patient Case Study #2

CA-4948 modifies disease in patient with FLT3 mutation

Disease	AML	
Dose	400 mg BID	
ECOG Status	2	
Prior Lines of Therapy	2	decitabine + venetoclax gilteritinib + hydroxyurea
Known Mutations	**FLT3-ITD**, RUNX1, ASXL1, BCOR, CSF3R, CEBPA, EZH2, NRAS, STAG2, TET2	
Cytogenetic Risk	ELN: Adverse	
Best Response	PR, FLT3 mutation eradicated	

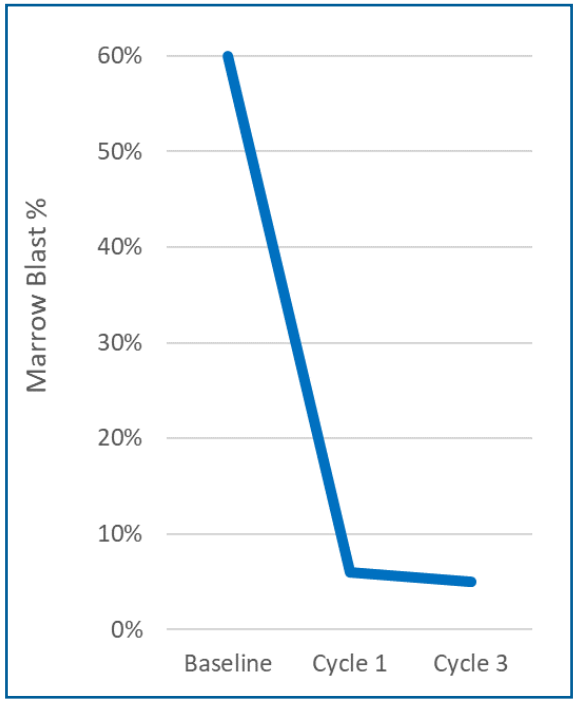
Refractory Disease
not responsive to prior therapy

FLT3 patient
who did not respond to
treatment with gilteritinib

(approved FLT3 inhibitor)

after 2 cycles of CA-4948,
FLT3 mutation
has been eradicated

Marrow Blast Reduction
deepened after several cycles



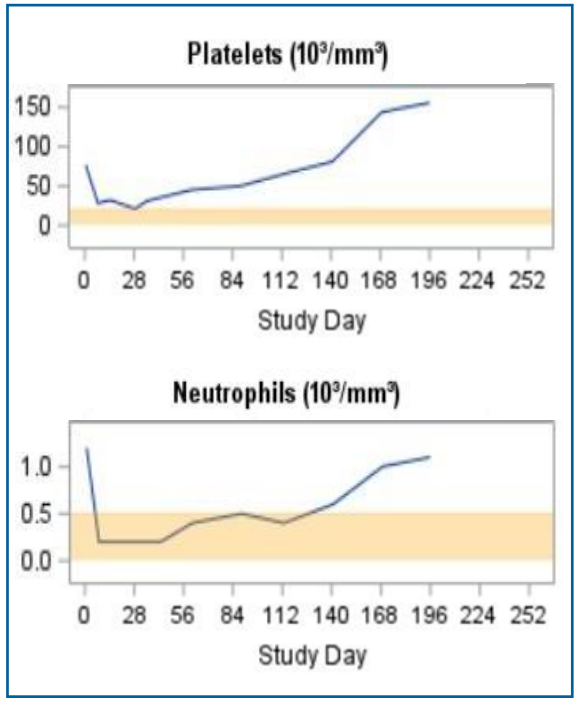
- New patient data reported at EHA 2021
- History of refractory disease to prior treatments, including both FLT3i and HMA
- FLT3 mutation, present at screening, completely eradicated after 2 cycles of treatment with CA-4948
- Supports rationale of expansion cohort in monotherapy for sub-population of patients with FLT3 mutation

Patient Case Study #3

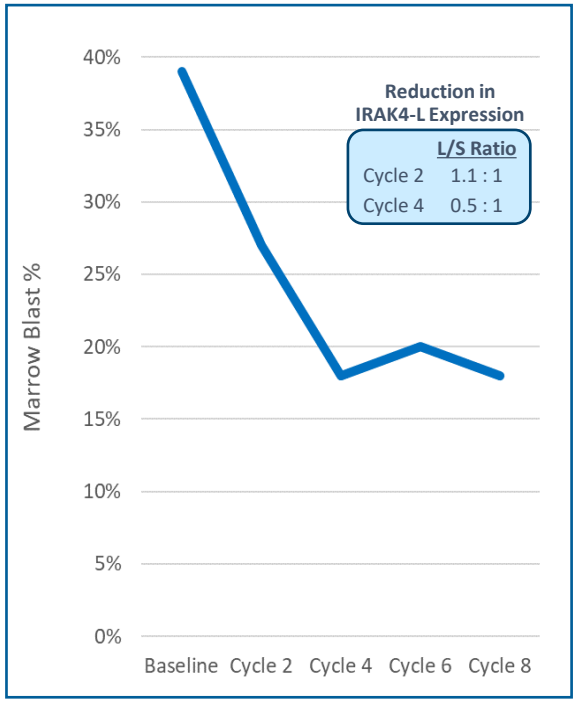
CA-4948 improves heme measures in patient with partial blast reduction

Disease	AML	
Dose	300 mg BID	
ECOG Status	0	
Prior Lines of Therapy	4	cytarabine + daunorubicin cytarabine + idarubicin cytarabine + mitoxantrone cytarabine
Known Mutations	IDH2, CBLC, DNMT3A, SMC1A, STAG2, ETV6	
Cytogenetic Risk	ELN: N/A	
Best Response	SD	

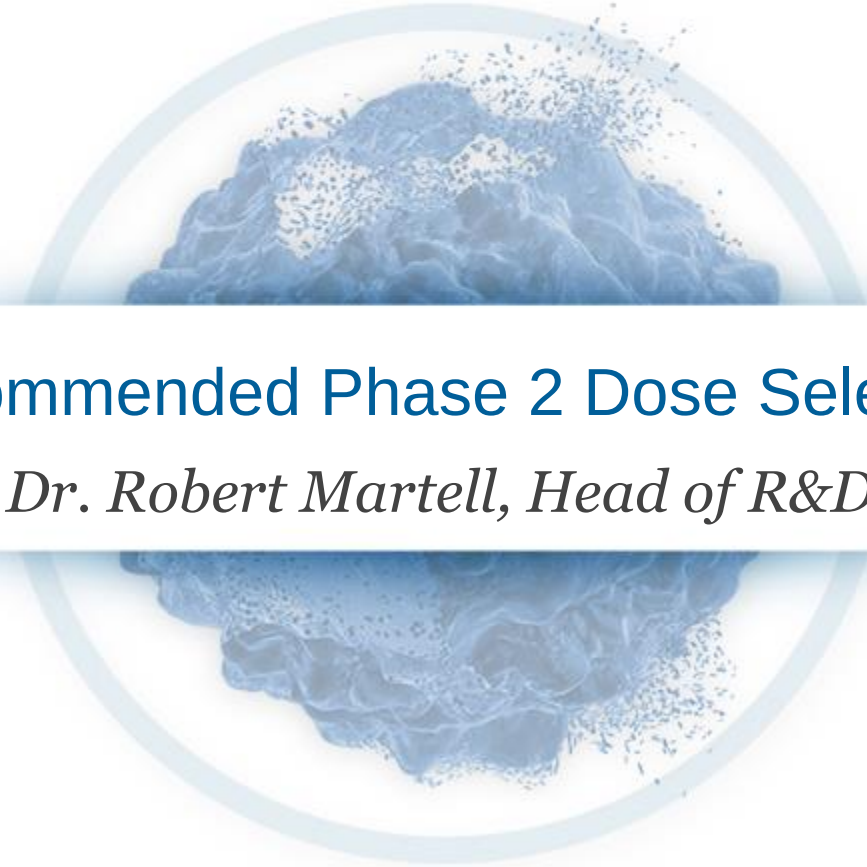
Heme Improvement indicates clinical benefit



Marrow Blast Reduction deepened after several cycles



- New patient data reported at EHA 2021
- Heme improvement seen in heavily pre-treated patient
- Reduction in IRAK4-L expression demonstrates CA-4948 is disease-modifying
- Supports rationale of expansion cohort in combination therapy



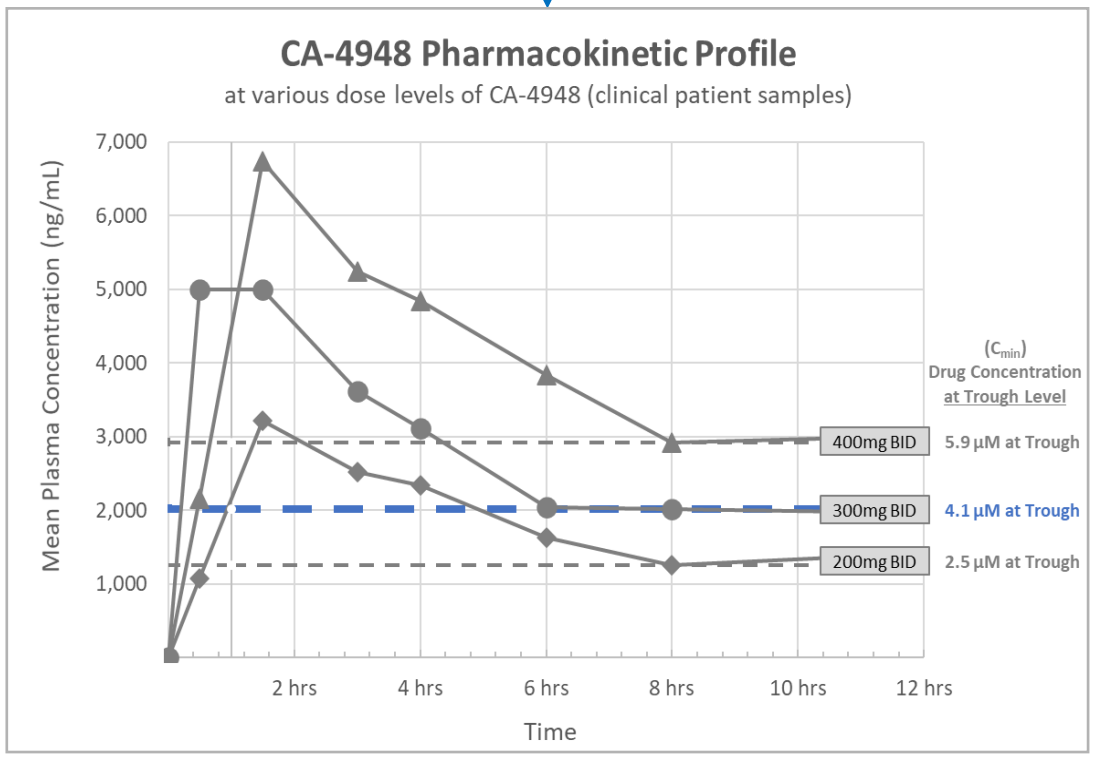
Recommended Phase 2 Dose Selection

Dr. Robert Martell, Head of R&D

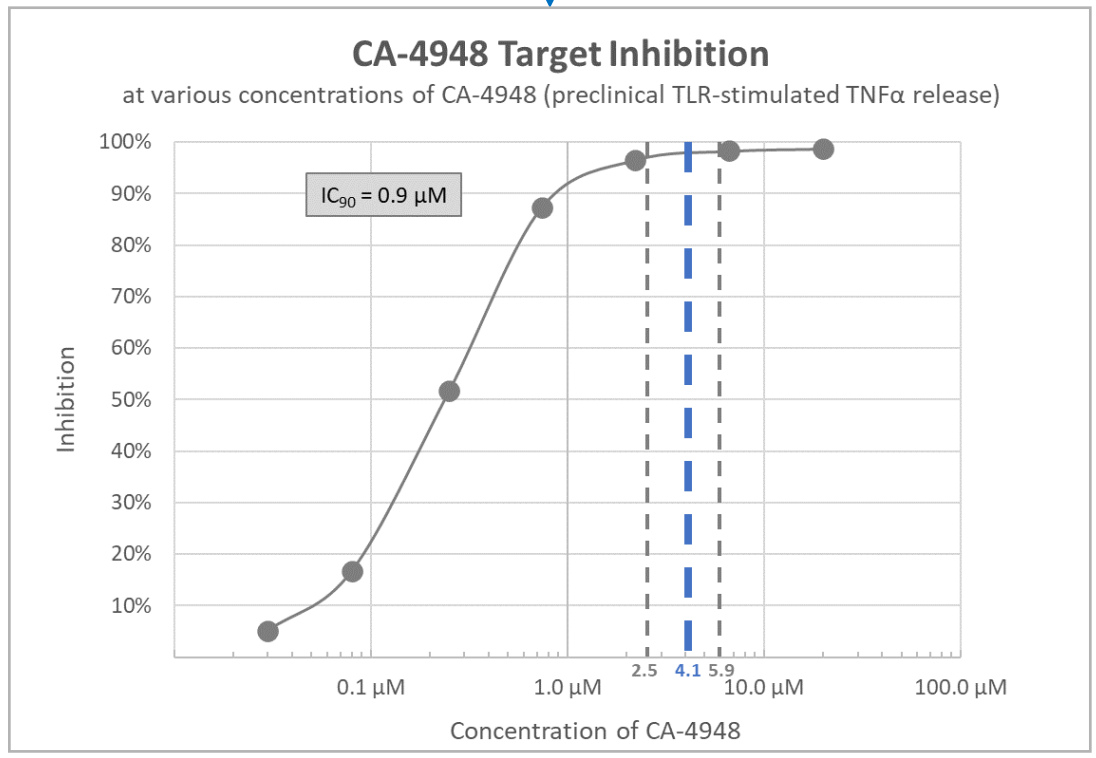
CA-4948 Target Inhibition by Dose

PK exposure correlates with 98% target inhibition

Trough Exposure	Dose	Inhibition
2.5µM	200mg	97%
4.1µM	**300mg**	**98%**
5.9µM	400mg	98%



Data from CA-4948 lymphoma clinical study



Data from preclinical study of target inhibition

Recommended Phase 2 Dose: 300mg BID

Confirmation of same dose used in the ongoing Lymphoma and lrMDS studies

PK/PD

- PK supports BID dosing with half-life of ~6 hours
- PK exposure correlates with 98% target inhibition

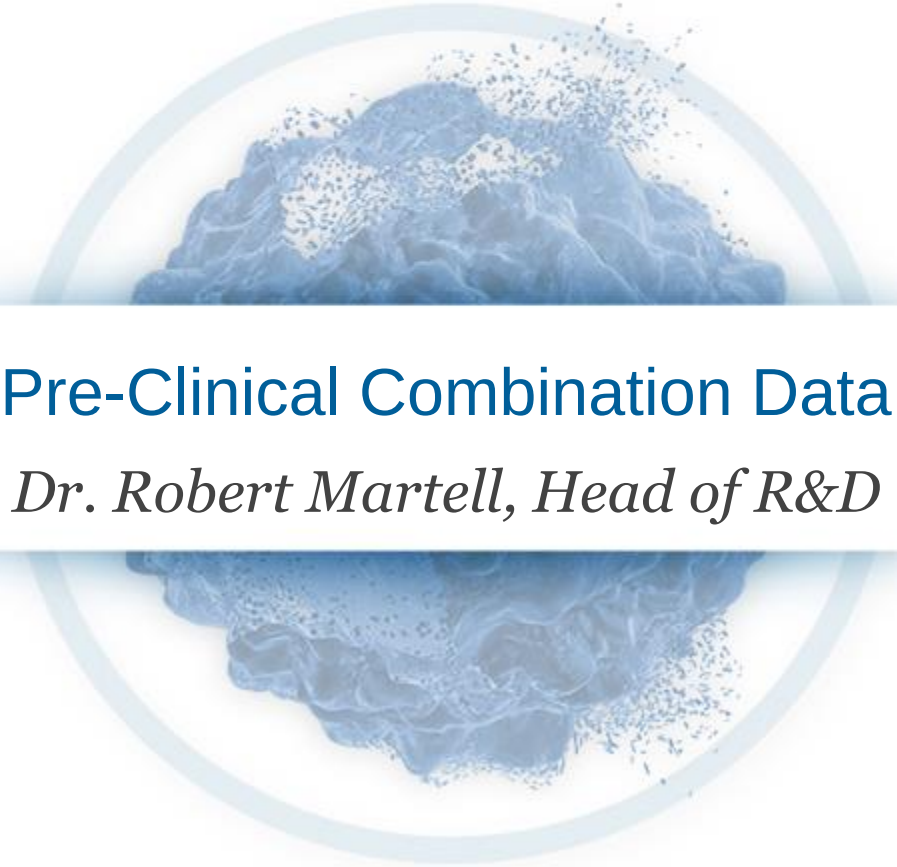
Safety

- Favorable safety and tolerability profile (no DLTs)
- No cumulative toxicity after 2 years of clinical study in NHL

Efficacy

- Blast reduction in 4 of 4 evaluable patients with elevated blast counts at baseline, including a CRi with negative MRD
- Durability demonstrated with initial patients still on study after 7-8 months

Recommended Phase 2 Dose = 300 mg BID (twice daily)



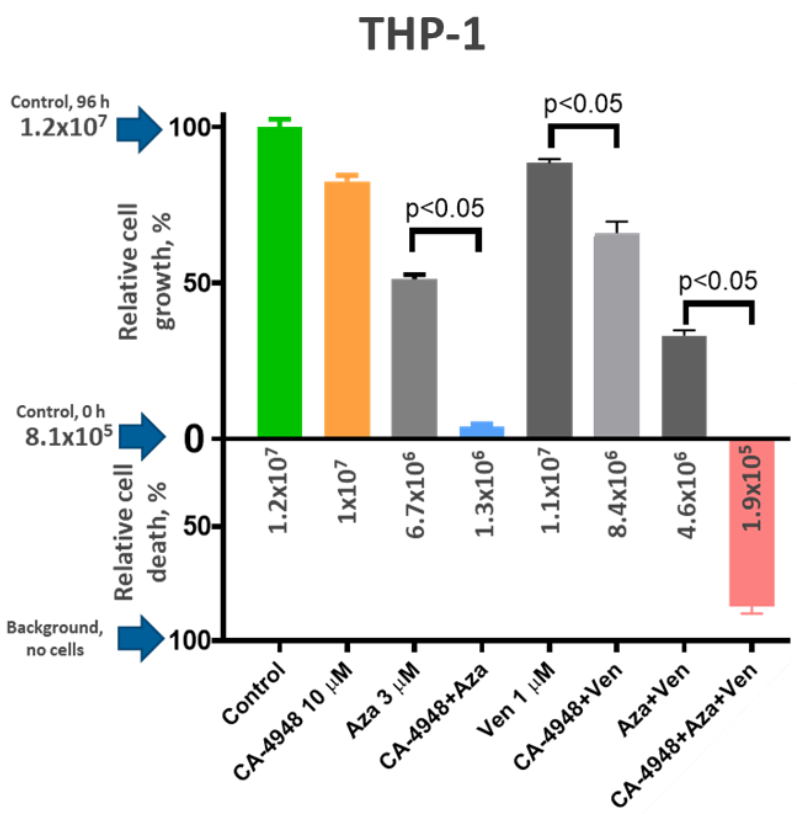
Pre-Clinical Combination Data

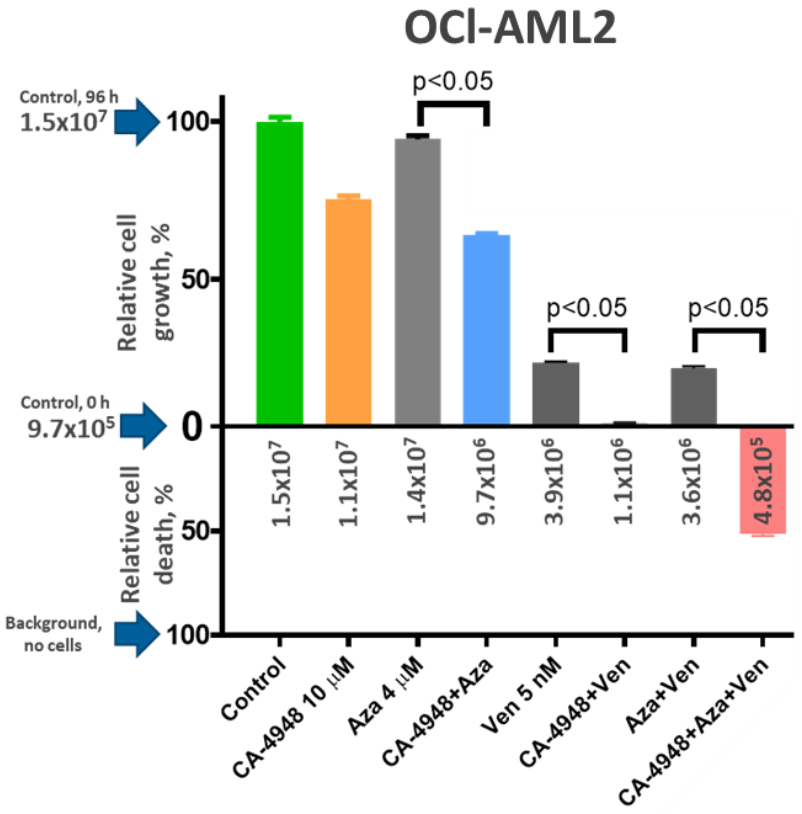
Dr. Robert Martell, Head of R&D

CA-4948 in AML/MDS

Preclinical data support study of CA-4948 in combination with azacitidine and venetoclax

Synergistic activity in leukemia cells provides a strong rationale for clinical testing of CA-4948 + azacitidine, CA-4948 + venetoclax, and the triplet combination of all three agents together in patients with AML





Summary Comments

James Dentzer, President & CEO


CURIS
Q&A