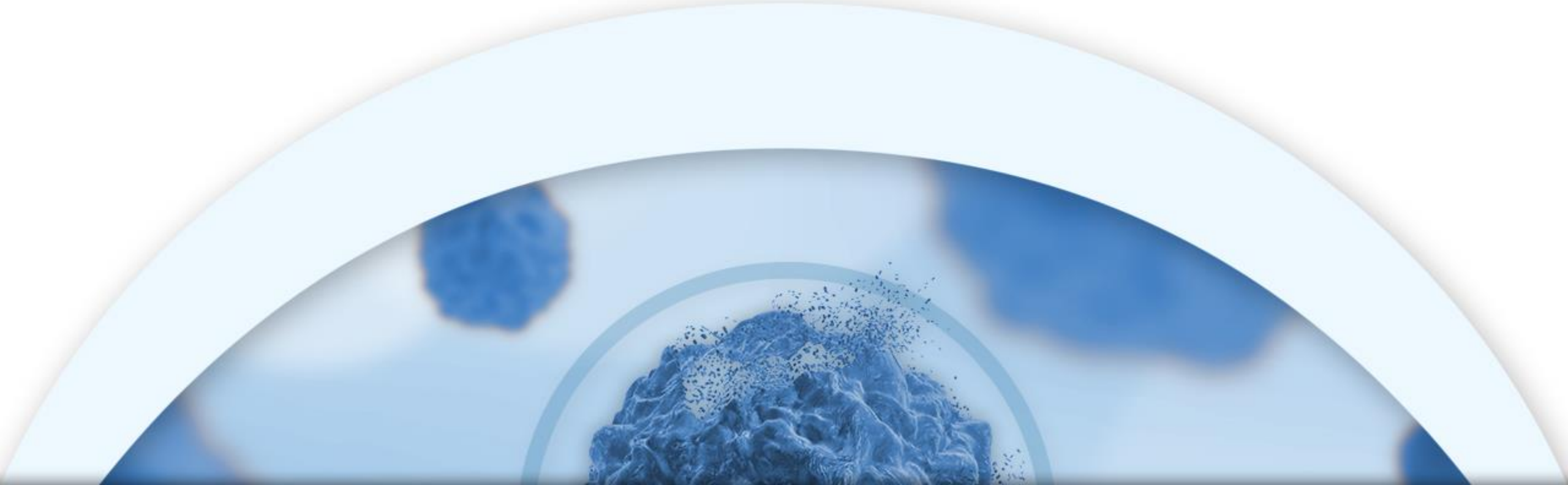
Corporate Presentation

NASDAQ: CRIS

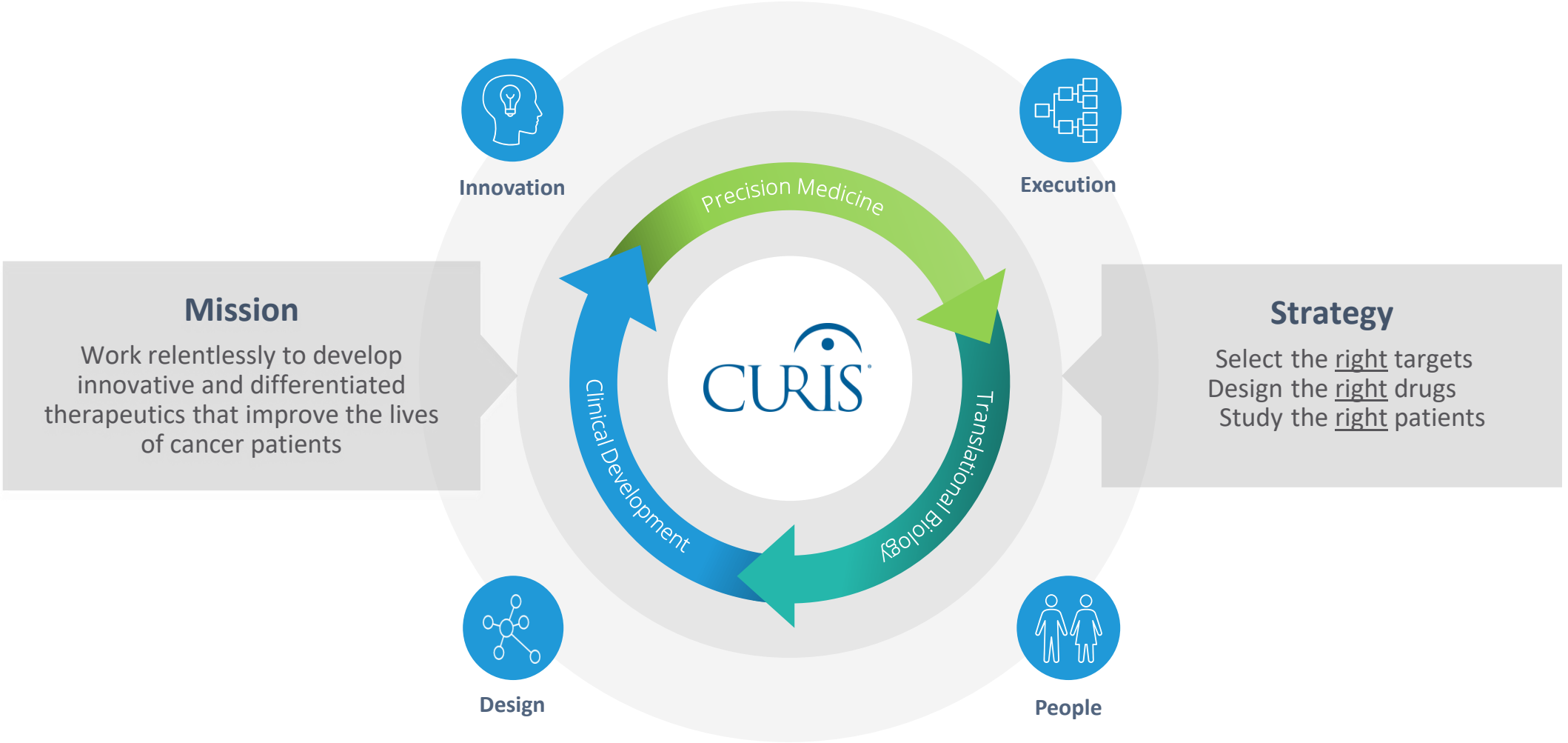


Cautionary Note Regarding Forward Looking Statements

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, statements with respect to the timing and results of future clinical and pre-clinical milestones; the timing of future preclinical studies and clinical trials and results of these studies and trials; the clinical and therapeutic potential of our drug candidates; and management’s ability to successfully achieve its goals. 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.

Curis Mission & Strategy

Developing the New Generation of Targeted Cancer Drugs



Mission

Work relentlessly to develop innovative and differentiated therapeutics that improve the lives of cancer patients

Strategy

Select the right targets
Design the right drugs
Study the right patients

Company

Overview

Investment Thesis	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need
Robust Pipeline	CA-4948: first-in-class inhibitor of IRAK4 in oncology *There are no drugs currently approved for IRAK4 inhibition in oncology* CI-8993: first-in-class antagonist of VISTA *There are no drugs currently approved for VISTA inhibition*
Corporate	• Experienced management team with proven capabilities • Curis R&D pioneered the first-in-class inhibitor of the Hedgehog pathway (Erivedge®) partnered with and commercialized by Genentech/Roche for advanced basal cell carcinoma • Cash and investments of approximately $168M as of Mar 31, 2021; cash runway into 2024

Evolution of Curis

Progressing through Clinical Studies on the Path to Potential Registration

2019 | **2020** | **2021**

Initial Clinical Data

- ☑ Report initial Ph1 data for CA-4948 in NHL
- ☑ Evaluate new published research in IRAK4-L expression and the potential opportunity for CA-4948 in AML/MDS

Expand Clinical Opportunities

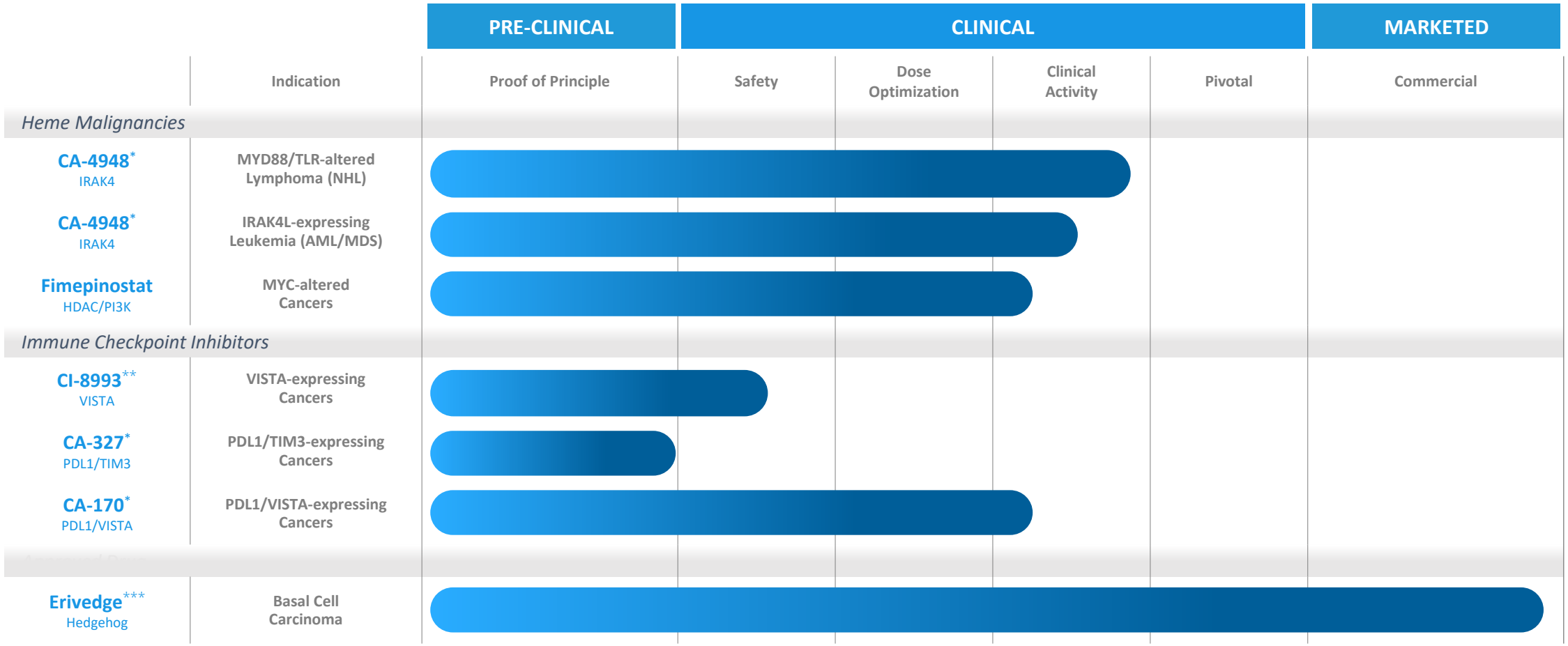
- ☑ Report expanded Ph1 data for CA-4948 study in NHL and identify Recommended Phase 2 Dose (RP2D)
- ☑ Initiate a Ph1 study of CA-4948 in AML/MDS including patients expressing IRAK4-L and report initial Ph1 data
- ☑ Acquire exclusive option to license the leading VISTA monoclonal antibody program (CI-8993) and initiate a Ph1 study

Registrational Strategy

- ☑ Initiate Combination Study of CA-4948 and ibrutinib in NHL and evaluate potential paths for registration
- ☑ Initiate the clinical and non-clinical research collaboration with the NCI under the CRADA for CA-4948
- ☑ Report expanded Ph1 data for CA-4948 study in AML/MDS and identify Recommended Phase 2 Dose (RP2D)
- ☐ Report initial clinical data for CI-8993 Ph1 study targeting VISTA in solid tumors

Pipeline

All Curis programs are novel, first-in-class



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IRAK4 Targeted Program in AML/MDS

CA-4948: In development for treatment of cancers driven by IRAK4-L

CA-4948 Overview

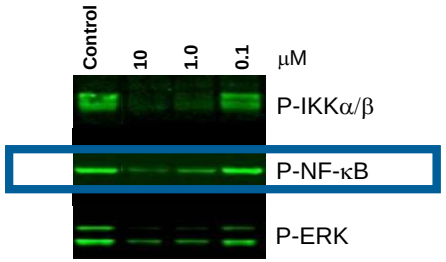
First-in-Class Inhibitor of IRAK4 in Oncology

In Nov 2020, the NCI selected CA-4948, Curis's first-in-class IRAK4 inhibitor, and entered into an agreement ("CRADA") with Curis to conduct both clinical and non-clinical studies of CA-4948 in oncology

Profile	
Value Proposition	• First-in-class IRAK4 inhibitor in cancer • Specific malignancies in Lymphoma are characterized by overactivity of NF-κB and the TLR/myddosome (which is dependent upon IRAK4) • Specific malignancies in Leukemia are characterized by spliceosome mutations that cause an overexpression of IRAK4-L (the oncogenic isoform of IRAK4) • Composition-of-matter IP extends into 2035
Target Patient Population	Lymphoma: 100% of patients treated w/ibrutinib (IRAK4i combination with BTKi) Leukemia: >50% of AML/MDS patients (population which overexpresses IRAK4-L)
Product Candidate Description	• Potent and orally bioavailable inhibitor of IRAK4 for treatment of NF-κB driven lymphomas and IRAK4-L driven leukemia

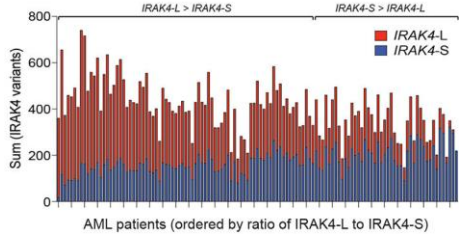
Kinase	K_d (nM)
IRAK4	23
IRAK1	12,000
IRAK2	>20,000
IRAK3	8,000
FLT3	31

Highly specific and targeted inhibitor of IRAK4 and other relevant kinases[1]



Phospho-protein levels in AML cells after treatment with CA-4948

In Lymphoma:
Potent suppressor of NF-κB signal transduction[2]

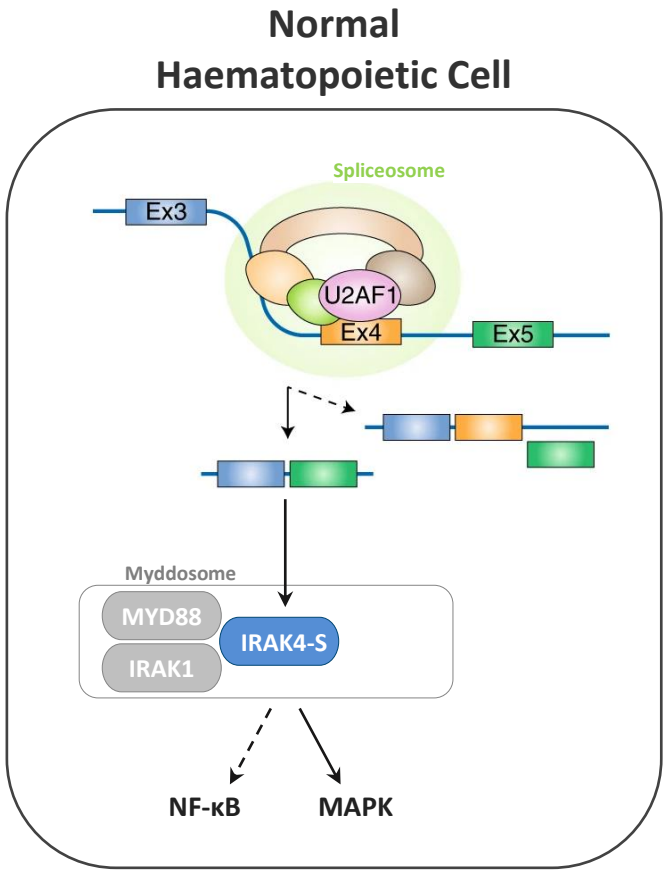


In Leukemia:
>50% of patients with AML overexpress IRAK4-L (long-to-short ratio of > 1.25)[3]

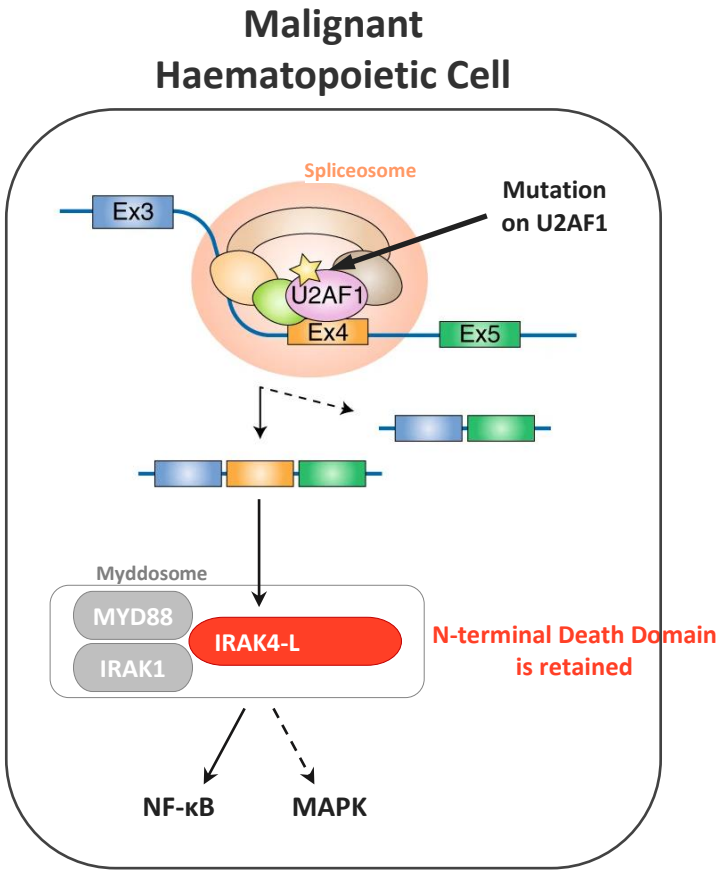
1) Booher et al. EHA 2019 (poster #PS991)
2) Booher et al. AACR 2017 (poster #1168)
3) Smith et al. Nat Cell Biol 2019

CA-4948 in AML/MDS

IRAK4-L is a Novel Target in AML/MDS



Guillamot et al. Nat Cell Biol. 2019



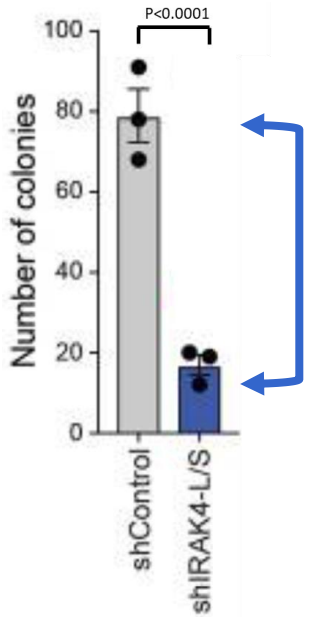
Guillamot et al. Nat Cell Biol. 2019

specific genetic mutations (incl. U2AF1 and SF3B1) drive the expression of IRAK-L, the long isoform of IRAK4

CA-4948 in AML/MDS

Targeting IRAK-L Demonstrates Anti-Cancer Activity in Preclinical Models

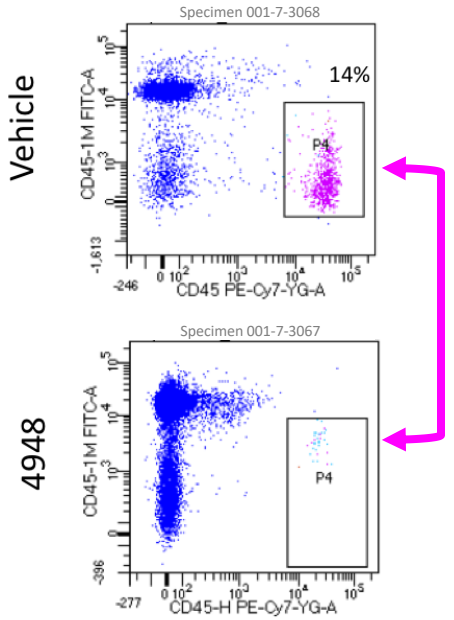
IRAK4-L is Oncogenic



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]

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 in AML/MDS

Landscape of Disease Targets in AML/MDS

Disease Driver	% of Patient Population
IRAK4-L	> 50%[1]
FLT3	25-30%[2]
TET2	10-20%[3]
IDH2	9-13%[4]
IDH1	6-10%[4]
CEBPA	~10%[3]

- Non-targeted therapies administered in monotherapy have historically provided limited clinical benefit, especially in relapsed/refractory patients
- Targeted therapies (e.g., FLT3, IDH) have been limited by the size of their respective target patient populations
- IRAK4-L is a novel target in AML/MDS and has been shown to be preferentially expressed in >50% of the AML/MDS patient population (>50% of patients have an IRAK4 long-to-short ratio > 1.25) [1]

1) Smith et al. Nat Cell Biol 2019
2) Saygin, et al. J Hematol Oncol. 2017 Apr 18
3) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6142505/
4) DiNardo et al. N Engl J Med 2018

CA-4948 in AML/MDS

Trial Design and Patient 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

Data cut-off: 30Apr2021

Study Objectives

Primary: Maximum tolerated dose and recommended Phase 2 dose

Secondary: Pharmacokinetic (PK) profile, preliminary anti-cancer activity

Study Population

- Relapsed/Refractory disease
- Histopathologically confirmed AML or High-Risk MDS
- Age ≥ 18 years
- ECOG performance Status of ≤ 2

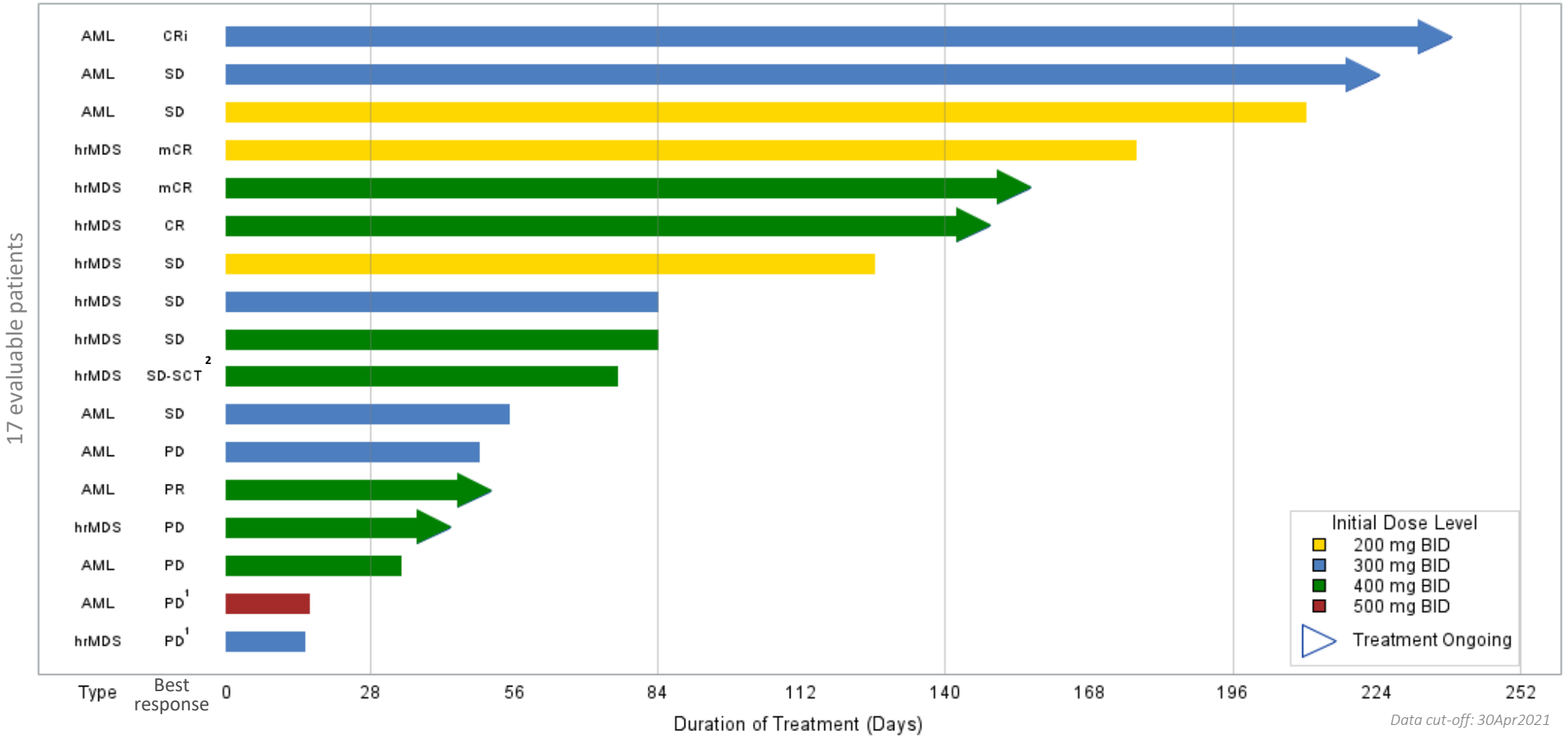
Dosing

- Oral
- 28-day cycles
- 3+3 escalation design (200mg BID, 300mg BID, 400mg BID and 500mg BID)

CA-4948 in AML/MDS

Treatment duration and patient response

5 objective responses and 1 patient who proceeded to SCT



Data cut-off: 30Apr2021

Best Response

hrMDS (n=9)

CR	1
mCR	2
SD	4
PD[1]	2

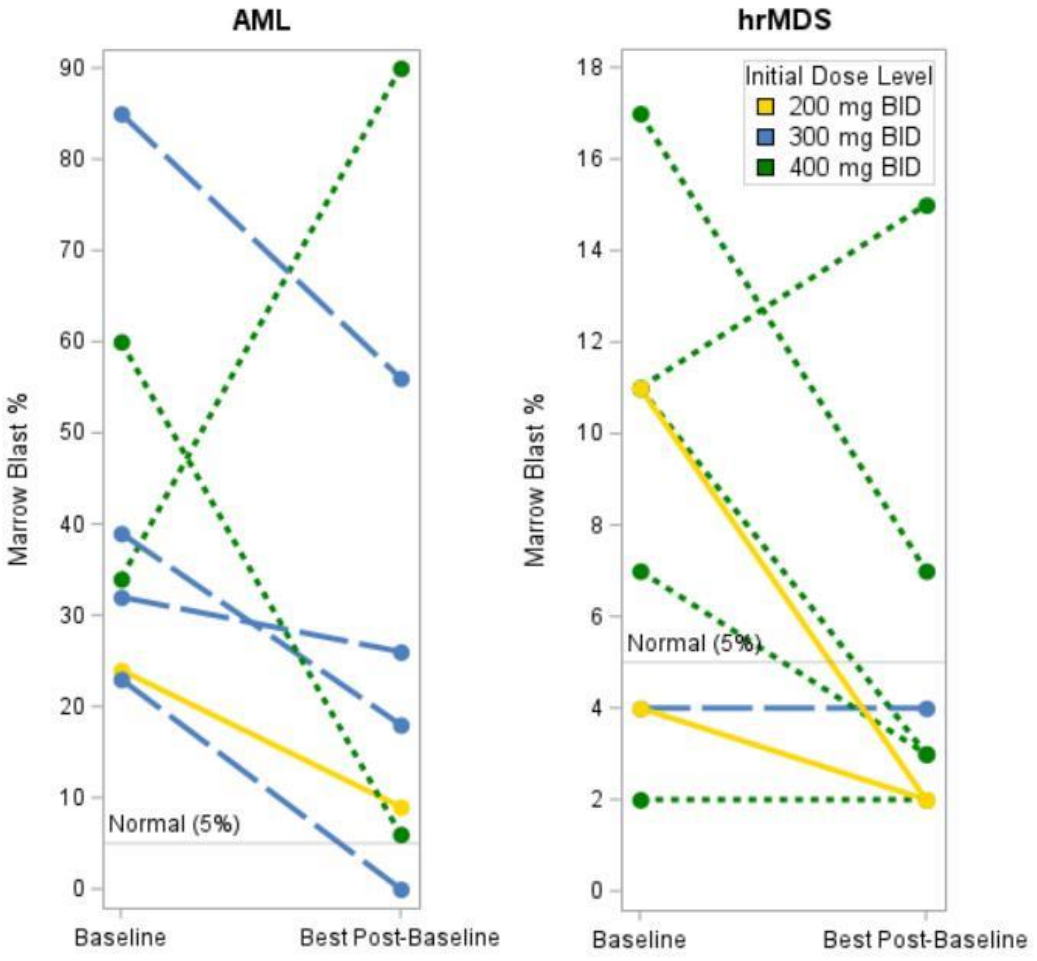
AML (n=8)

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)

CA-4948 in AML/MDS

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

Data cut-off: 30Apr2021

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

CA-4948 in AML/MDS

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 after 1 cycle (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

CA-4948 in AML/MDS

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

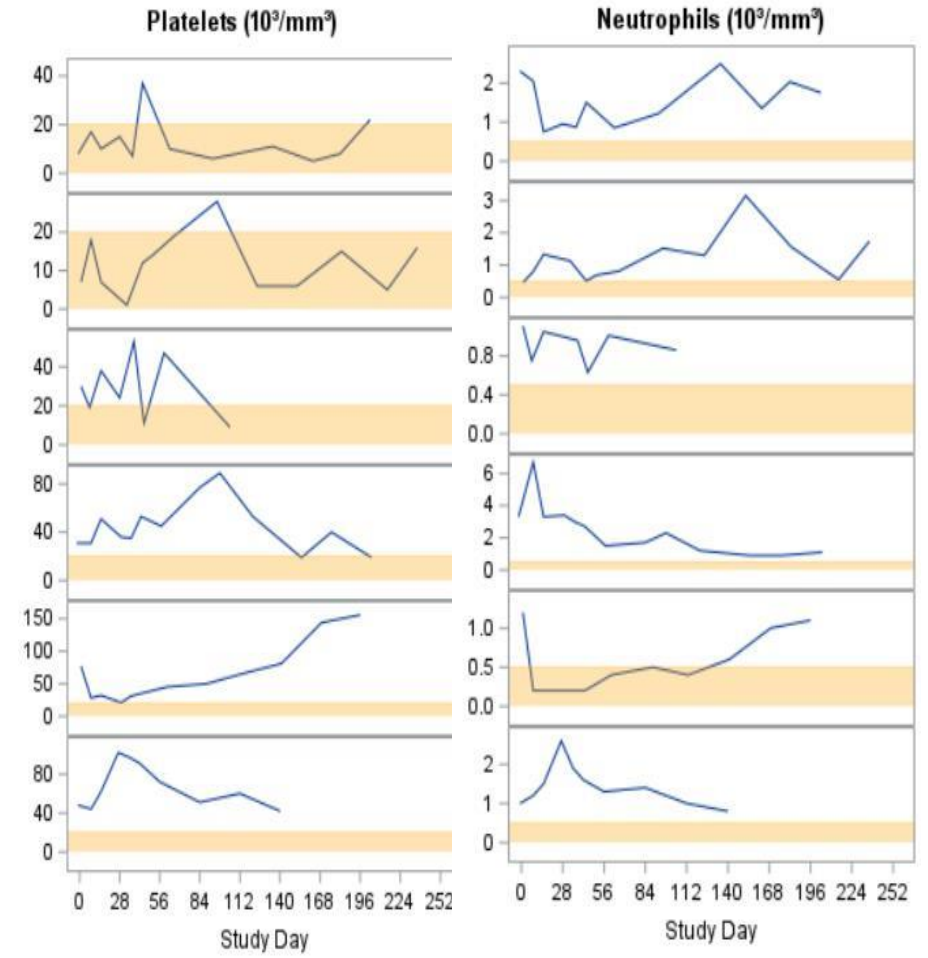
SD
63% blast reduction (24 to 9)
3 prior lines of therapy

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.

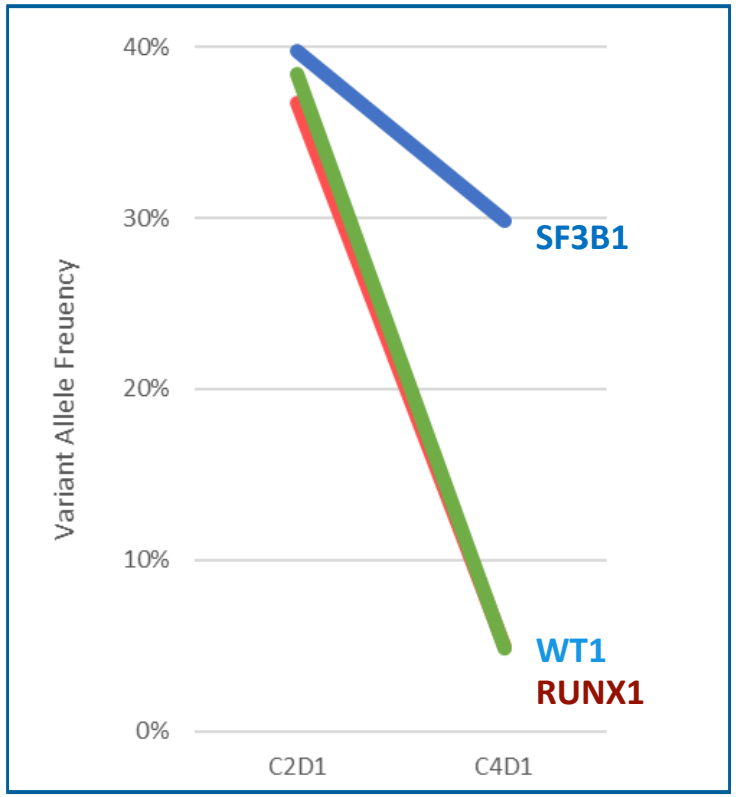
CA-4948 in AML/MDS

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

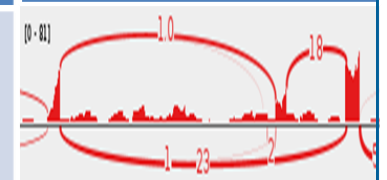
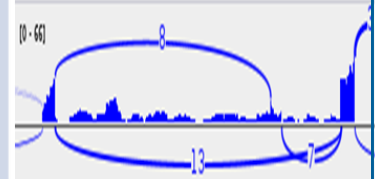
(NGS)

Patient DNA Sequencing



(RNA-seq)

Patient RNA Sequencing

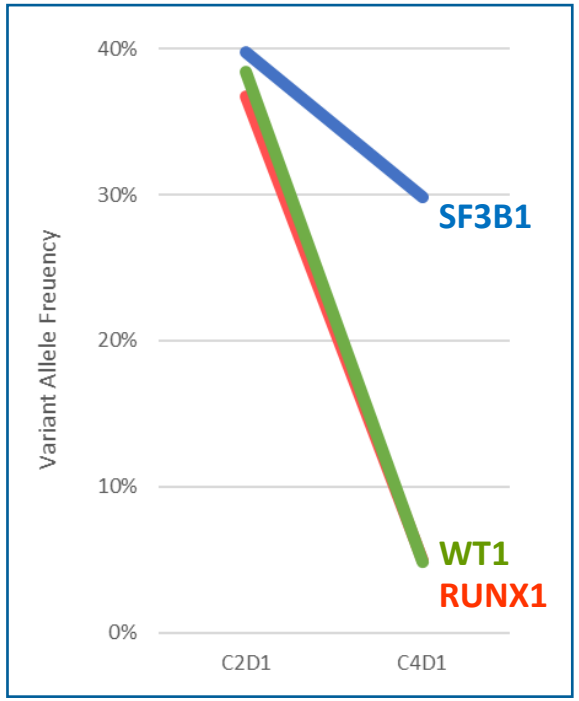
CA-4948 Tx Cycle	Long/Short Ratio	3 EXON 4 5
Control: Healthy CD34	18/23 (0.78)	
C2D1	8/7 (1.14)	
C4D1	7/13 (0.53)	

CA-4948 in AML/MDS: Patient Case Study #1

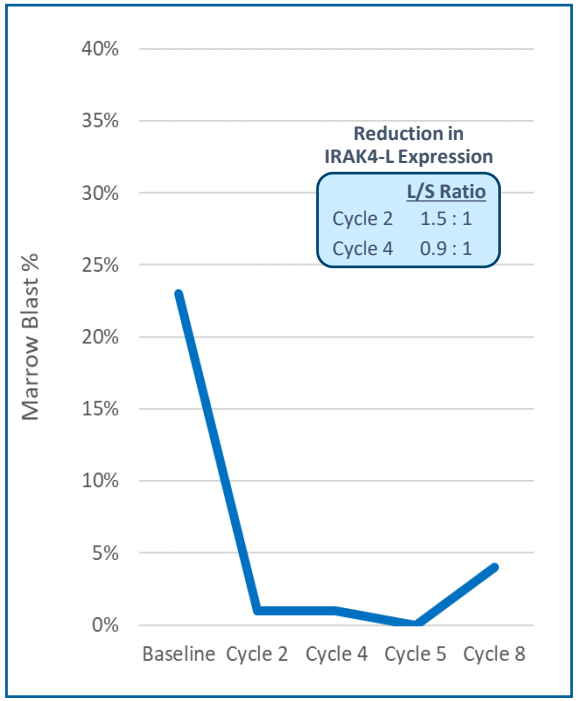
CA-4948 modifies disease in patient with spliceosome mutation

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

CA-4948 in AML/MDS: 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	

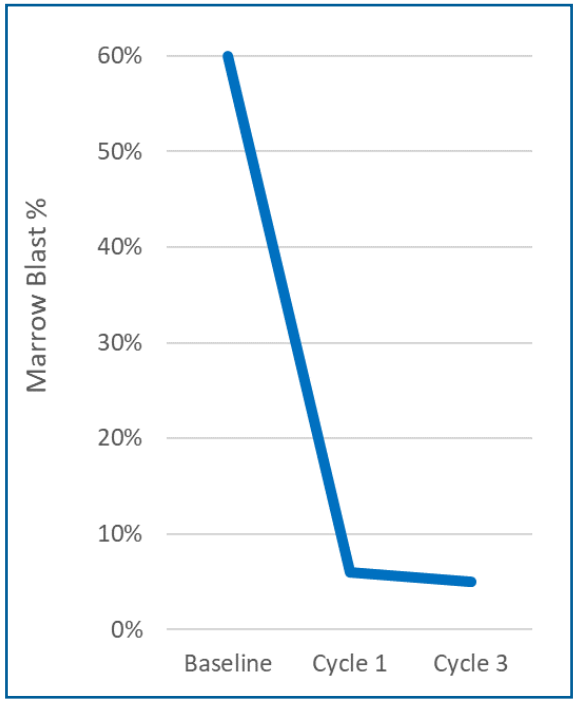
Refractory Disease
not responsive to prior therapy

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



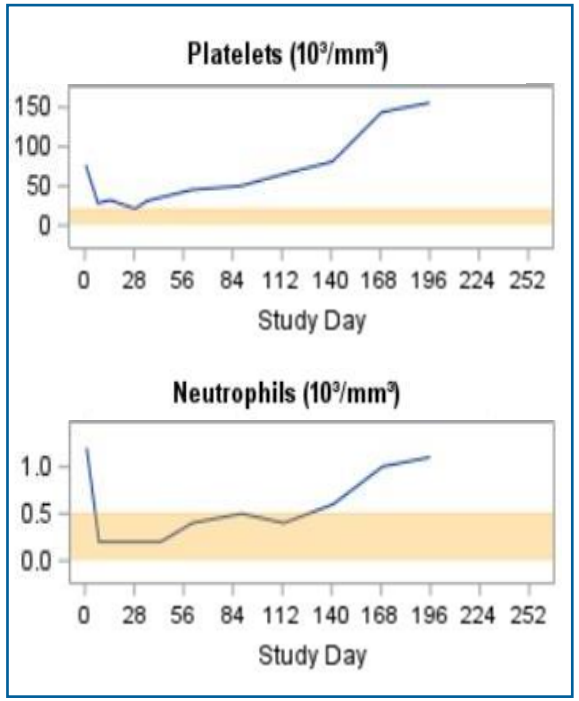
- New patient data reported at EHA 2021
- History of refractory disease to prior treatments, including both FLT3i and HMA
- FLT3 mutation, present at screening, completely eradicated after 2 cycles of treatment with CA-4948
- Supports rationale of expansion cohort in monotherapy for sub-population of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

CA-4948 in AML/MDS: Patient Case Study #3

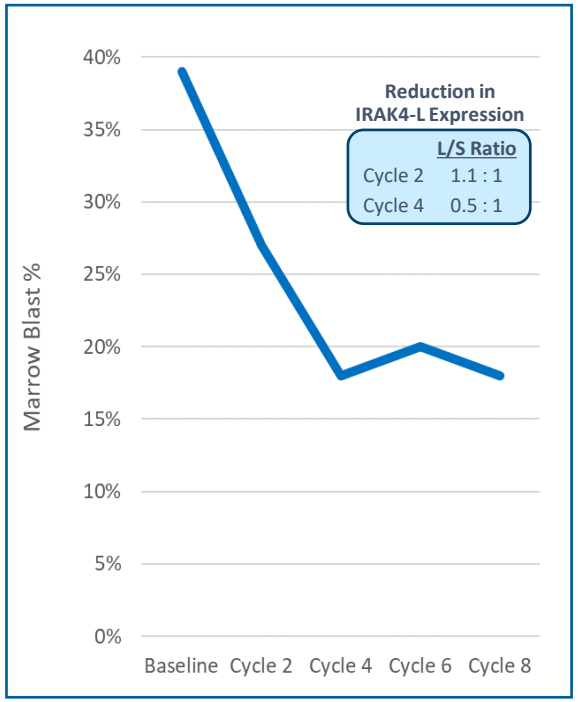
CA-4948 improves heme measures in patient with partial blast reduction

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

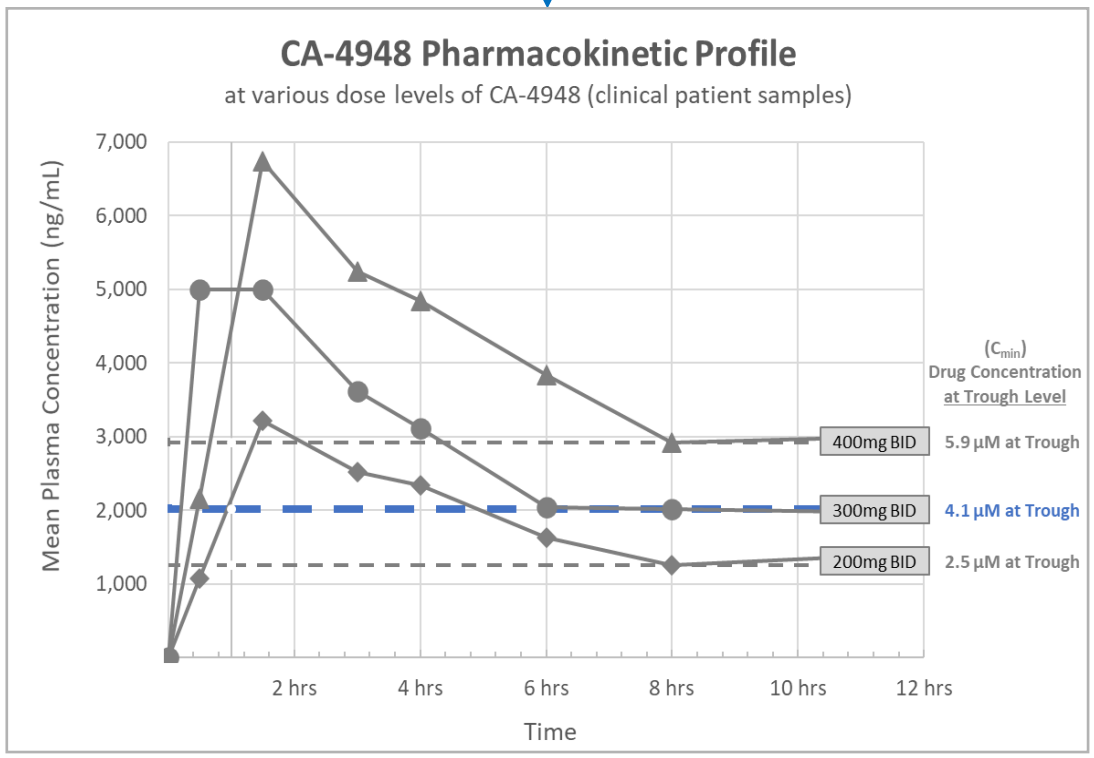


- New patient data reported at EHA 2021
- Heme improvement seen in heavily pre-treated patient
- Reduction in IRAK4-L expression demonstrates CA-4948 is disease-modifying
- Supports rationale of expansion cohort in combination therapy

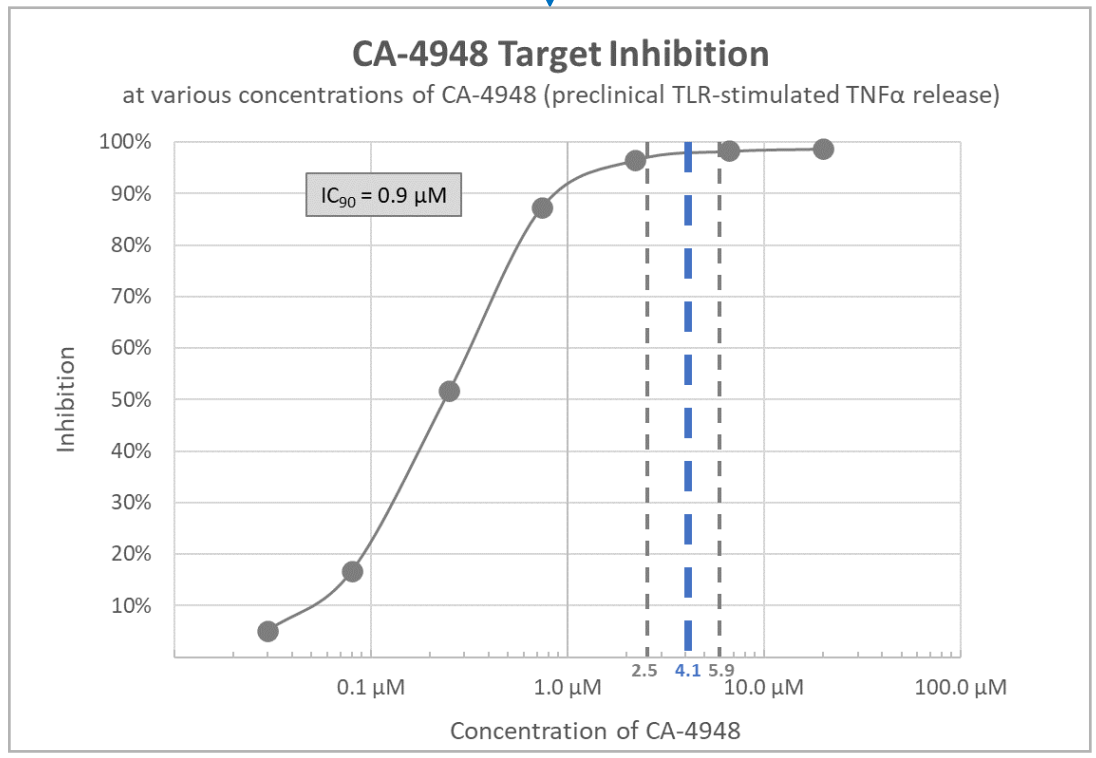
CA-4948 Target Inhibition by Dose

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

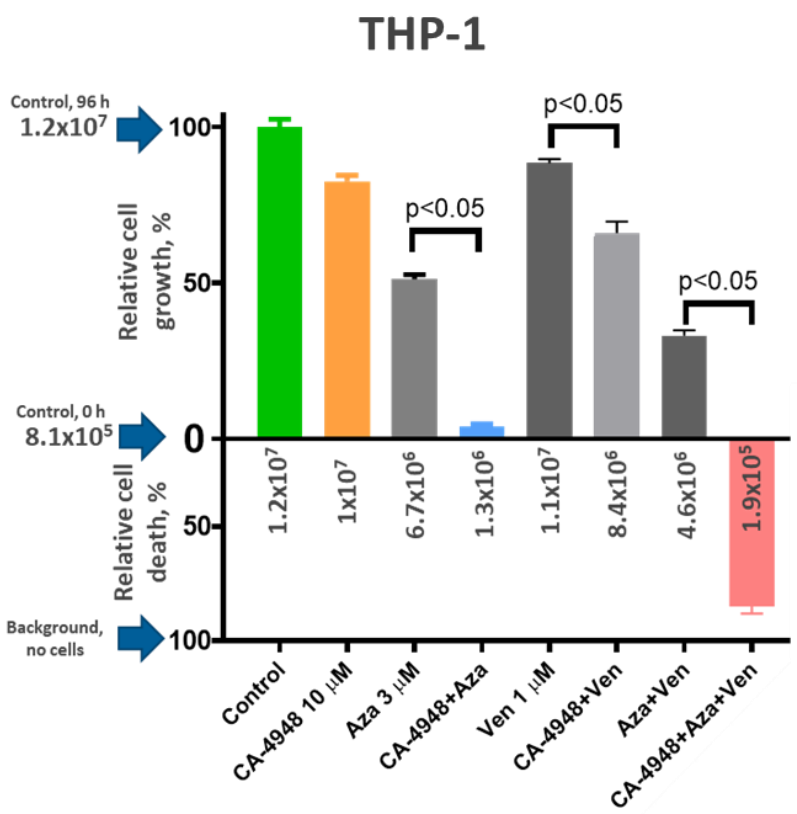
- Blast reduction in 4 of 4 evaluable patients with elevated blast counts at baseline, including a CRi with negative MRD
- Durability demonstrated with initial patients still on study after 7-8 months

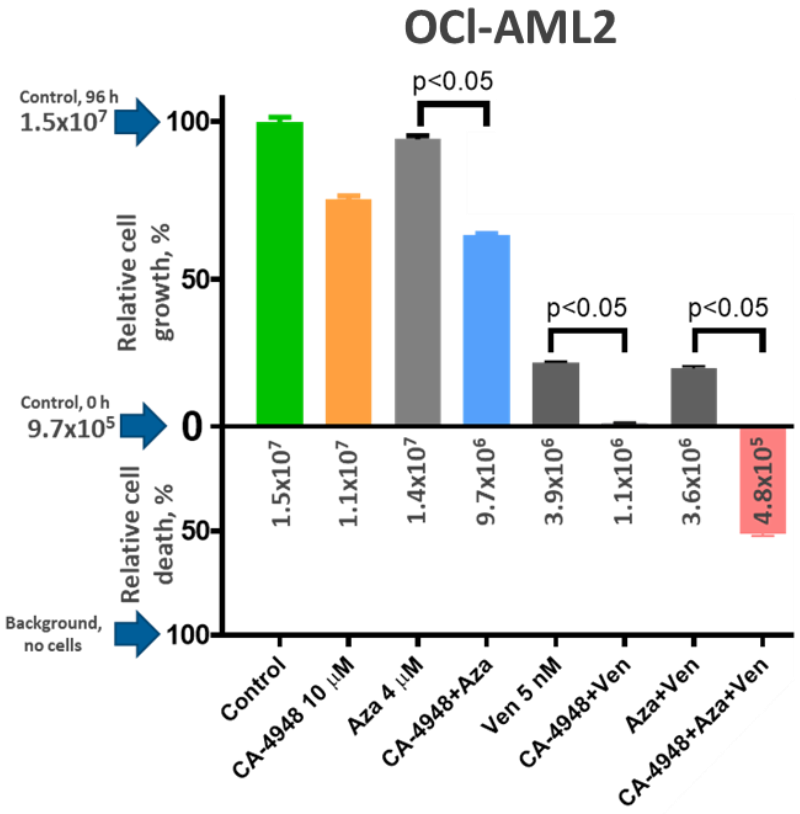
Recommended Phase 2 Dose = 300 mg BID (twice daily)

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





CA-4948 in AML/MDS

Identifying the patient population that may benefit from treatment with CA-4948

ASH 2019	ASH 2020	EHA 2021
Preclinical Data	6 patients Initial Clinical Data	22 patients Clinical Update
Combination therapy for ~50% of patients	**Combination therapy for all comers** **Potential accelerated regulatory path for sub-population**	**Combination therapy for all comers** **Potential accelerated regulatory path for spliceosome and FLT3 populations**
Seminal paper identifies the long isoform of IRAK4 as the key oncogenic driver in AML/MDS[1] Blast count reduction observed in cells with IRAK4 long/short ratio of ≥ 1.25:1 (~50% of AML/MDS patients have this ratio)	All evaluable patients achieve blast reduction* with 2 objective responses ○ IRAK4 inhibition more successful in patients than in the lab (expands potential opportunity from 50% to 100% of patients) ○ 2 objective responses indicates potential for accelerated approval in sub-population	10 of 12 evaluable patients achieve blast reduction* with 5 objective responses ○ All 3 patients with spliceosome mutation achieve objective response ○ Patient with FLT3 mutation achieves objective response and eradication of the FLT3 mutation DNA and RNA genomics analysis demonstrates disease-modifying activity

Next Steps in Expansion

Supporting Early-Line Opportunity:

- *Combination: CA-4948 + azacitidine*
- *Combination: CA-4948 + venetoclax*

Supporting Potential Rapid Approval:

- *Monotherapy: Spliceosome mutation*
- *Monotherapy: FLT3 mutation*

1) Smith et al. Nat Cell Biol 2019

**Evaluable patients include all patients who had elevated blast count at baseline (>5% blasts) for whom post-treatment marrow assessments were available as of the cutoff date*

IRAK4 Targeted Program in NHL

CA-4948: In development for treatment of cancers driven by NF-κB and the TLR/Myddosome

CA-4948

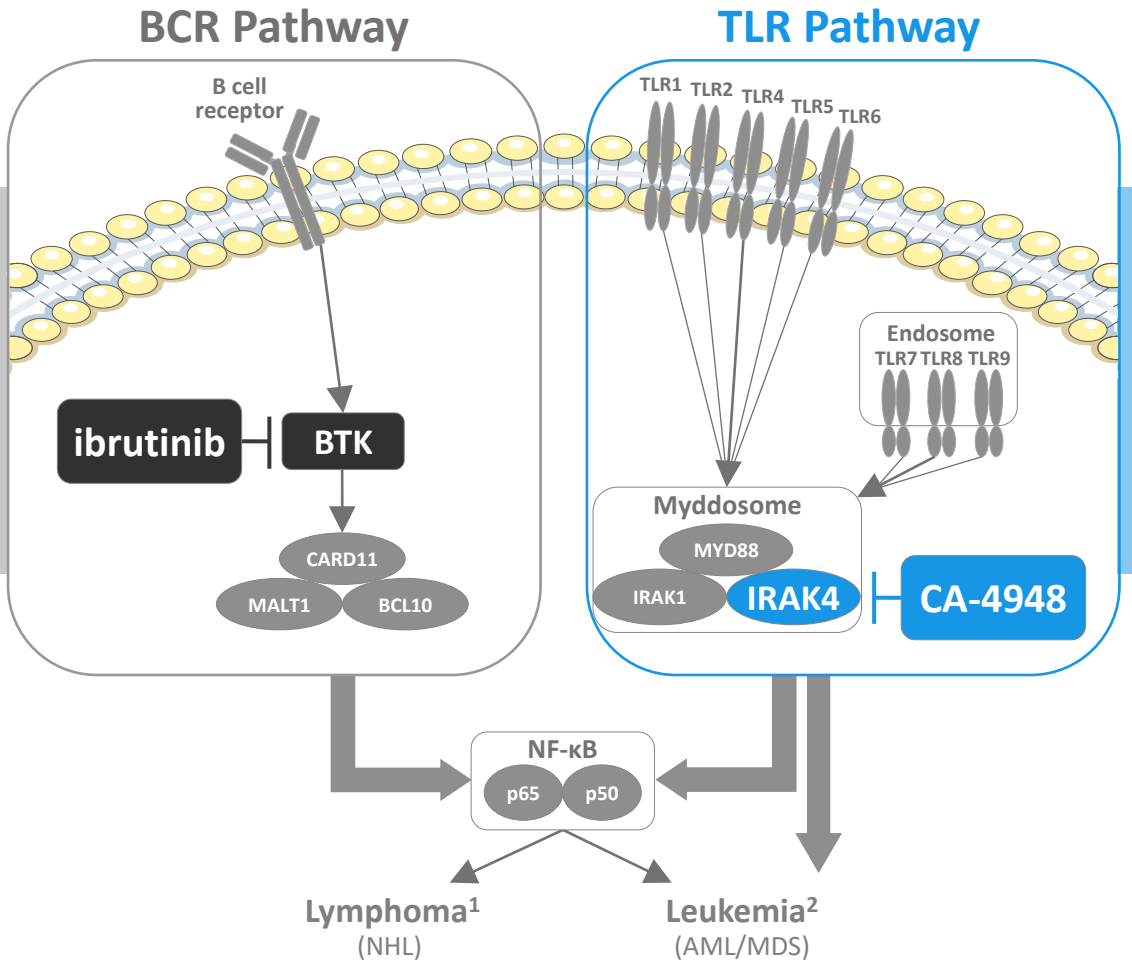
Novel Mechanism of Action for Addressing NF-κB

BCR and TLR are parallel pathways and primary independent activators of NF-κB

Pathway is Oncogenic

Pathway activates NF-κB

Pathway is dependent upon BTK



Pathway is Oncogenic[2,3,4]

Pathway activates NF-κB

Pathway is dependent upon IRAK4

–Signaling requires myddosome, which requires IRAK4

1) IMBRUVICA Package Insert. Rev 08/2018
2) Ngo et al. Nature. 2011 Feb 3;470(7332):115-9
3) Küppers et al. J Exp Med. 2015. 212(13): 2184
4) Smith et al. Nat Cell Biol 2019

CA-4948 in Lymphoma

Trial Design

Data cut-off: 23Nov2020

Baseline Characteristics of Ph1 Patients	Overall (N=31)
Male	26 (84%)
Female	5 (16%)
Median Age	69yrs
Histology	
Diffuse large B-cell lymphoma (DLBCL)	14 (45%)
Transformed follicular lymphoma (t-FL/DLBCL)	6 (19%)
Waldenström's Macroglobulinemia (WM)	4 (13%)
Other Lymphoma*	7 (23%)
Prior Therapies	
Median prior lines of therapy	4 prior lines
BTK inhibitor, n (%)	6 (19%)
CAR-T, n (%)	5 (16%)
ASCT , n (%)	7 (23%)
Other	13 (42%)
MYD88 Status	
Positive, n (%)	2 (6%)
Negative, n (%)	18 (58%)
Unknown, n (%)	11 (35%)

**includes Lymphoplasmacytic (n=2), Mantle Cell (n=2), Marginal Zone (n=2), High Grade MYC-BCL_6 (n=1)*

Study Objectives

Primary: Safety and tolerability

Secondary: Pharmacokinetic (PK) profile, preliminary anti-cancer activity

Study Population

- Relapsed/Refractory disease
- Histopathologically confirmed B-cell NHL, including WM/LPL
- Age ≥ 18 years
- ECOG performance status of ≤ 1

Dosing

- Oral, QD or BID continuous dosing
- 21-day cycles

Dose Levels, 3+3 Design

QD: 50, 100mg

BID: 50, 100, 200, 300 or 400mg

Treatment Emerging Adverse Events

Most AEs have been Grade 1-2, manageable, and reversible

	Adverse Reaction	200 mg BID (n=5); (%)		300 mg BID (n=6); (%)		400 mg BID (n=8); (%)		All (n=30); (%)
		All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades	Grade 3 or 4	All Grades
Gastrointestinal disorders	Diarrhea	20	0	33	0	25	0	20
	Nausea	20	0	17	0	38	0	27
	Vomiting	20	0	17	17	25	0	20
	Constipation	20	0	0	0	13	0	20
Respiratory	Upper respiratory infection	40	20	0	0	13	0	7
	Dyspnoe	20	0	0	0	13	13	7
	Upper-airway cough	40	0	0	0	0	0	7
General & Other	Fatigue	40	0	0	0	50	0	37
	Oedema	20	0	0	0	0	0	10
	Dehydration	20	0	0	0	13	13	10
Nervous system disorders	Headache	20	0	0	0	13	0	10
	Dizziness	0	0	0	0	25	0	20
	Insomnia	20	0	0	0	13	0	7
	Peripheral sensory neuropathy	0	0	0	0	25	0	7
Musculoskeletal disorders	Back pain	20	0	0	0	13	0	10
	Myalgia	40	0	0	0	38	0	17
	Rhabdomyolysis	0	0	0	0	25	25	7
	Muscle weakness	20	20	0	0	13	0	7
Hematological	Neutropenia	40	40	17	17	25	0	7
	Anemia	20	0	33	0	13	13	20
	Thrombocytopenia	0	0	0	0	13	13	7

Data cut-off: 11Oct2020

General

- No Grade 5 toxicity
- Only 2 treatment discontinuations due to TEAEs; both at low doses
- (asymptomatic amylase increase; rash)
- Intra-patient dose-reductions: 13%
- Intra-patient dose-escalations: 10%

Rhabdomyolysis

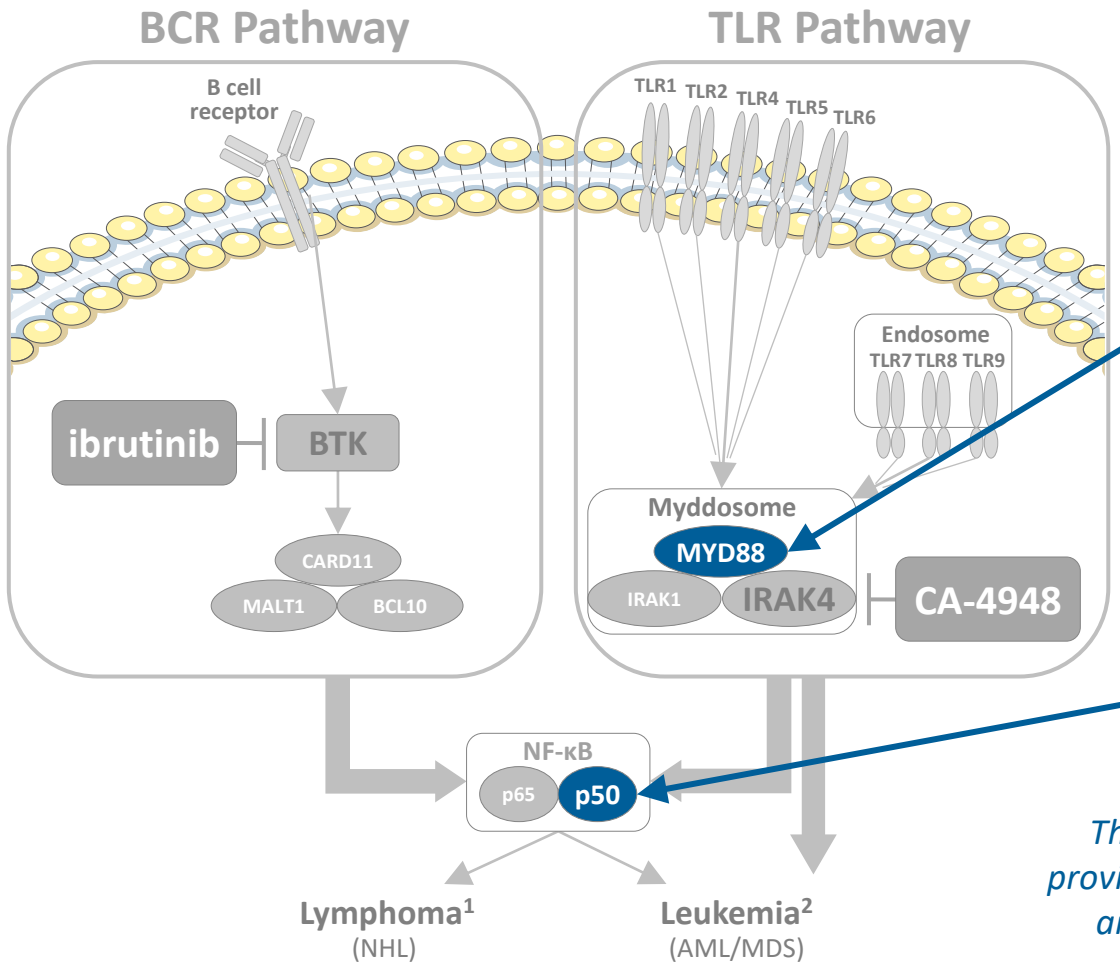
- Observed in 2 patients, based on muscle soreness and CPK elevation
- No renal dysfunction was observed
- Both cases observed in Cycle 1 of dosing, early monitoring of CPK required
- Additional risk factors may be present (vigorous exercise, dehydration, co-medications such as lipid-lowering statins)
- Requires dose interruption; treatment according to clinical presentation; in our uncomplicated cases, hydration, symptom control
- Both cases were reversible; treatment can be resumed at lower dose level

Other

- No TLS
- ECG – no significant changes from baseline; no delayed toxicity

CA-4948 in Lymphoma

Two Potential Biomarkers Identified



2

Is NF-κB activity driven by the TLR/myddosomal axis?

MYD88 Mutation

Genetic alteration of MYD88 at baseline causes constitutive activation of the myddosome and is a driver of NF-κB activity

This potential predictive biomarker may support patient enrichment by identifying patients with excessive myddosome activity (who may therefore be good candidates for IRAK4 inhibition)

1

Is NF-κB is active?

NF-κB phospho-p50

Positive expression of NF-κB phospho-p50 indicates that the NF-κB complex is active

This potential biomarker may support patient selection and provide evidence that CA-4948 is hitting the direct target (IRAK4) and inhibiting the downstream target (the NF-κB complex)

1) IMBRUVICA Package Insert. Rev 08/2018
2) Ngo et al. Nature. 2011 Feb 3;470(7332):115-9

CA-4948 in Lymphoma

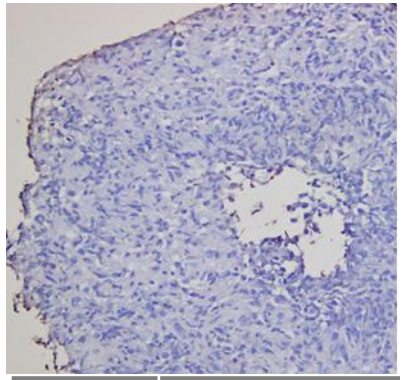
Early Biomarker Data from Phase 1 patients

This clinical study is ongoing, more data are needed to confirm these potential biomarkers

NF-κB phospho-p50

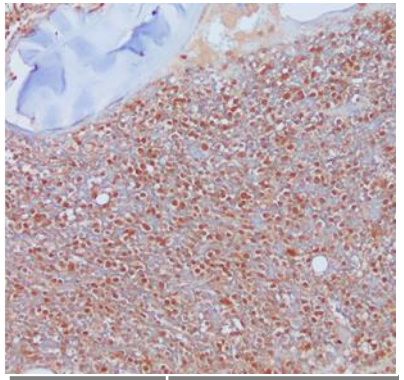
NF-κB phospho-p50 protein expression at baseline (indicator of NF-κB activity) correlates with patient outcomes

NEGATIVE at baseline
NFκB phospho-p50 expression before treatment with CA-4948



Patient	Best Response
12-1002	+86% PD
18-2004	+156% PD
02-4004	+75% PD
12-4004	+125% PD
12-5006	+190% PD
13-6001	+98% PD
01-4002	+7% PD

POSITIVE at baseline
NFκB phospho-p50 expression before treatment with CA-4948



Patient	Best Response
19-1001	-35% SD
02-1001	-24% SD
02-3003	+22% SD
12-5007	-35% SD
02-6007	+25% SD
02-6008	+16% SD
15-1001	+65% PD

Note: data included for all patients for whom pre/post samples were available as of Nov 23, 2020

p-p50 Biomarker May Support Patient Selection

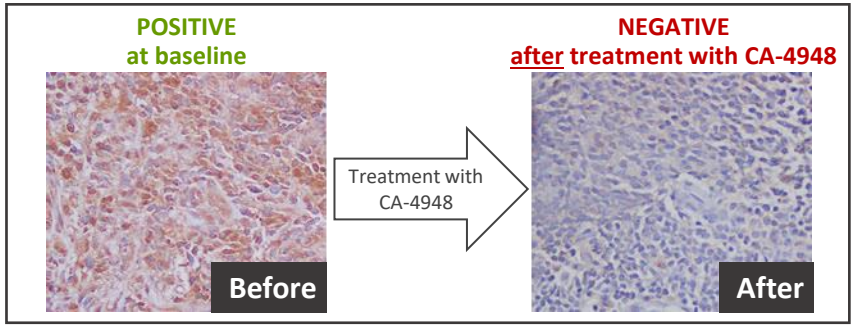
- Patients whose tumors do not exhibit NF-κB activity may not be amenable to NF-κB downregulation
  - *7 of 7 patients testing negative at baseline experienced disease progression*
  - *2 of these patients were dosed at 200mg BID*
- Patients whose tumors do exhibit NF-κB activity may be amenable to NF-κB downregulation
  - *6 of 7 patients testing positive for p-p50 at baseline achieved stable disease or tumor shrinkage*
  - *1 of these patients (012-5007) was dosed at 300mg BID*

MYD88 Biomarker May Support Patient Enrichment

- Both patients whose tumor tested positive for MYD88 mutation saw tumor reduction
- Observed tumor reduction is consistent with our thesis that patients with MYD88-mutated tumors should benefit from IRAK4 inhibition

Phospho-p50 Expression in Pre/Post Tumor Biopsies Also Provides Evidence that CA-4948 is Hitting the Target (IRAK4) and Downregulating NF-κB Activity

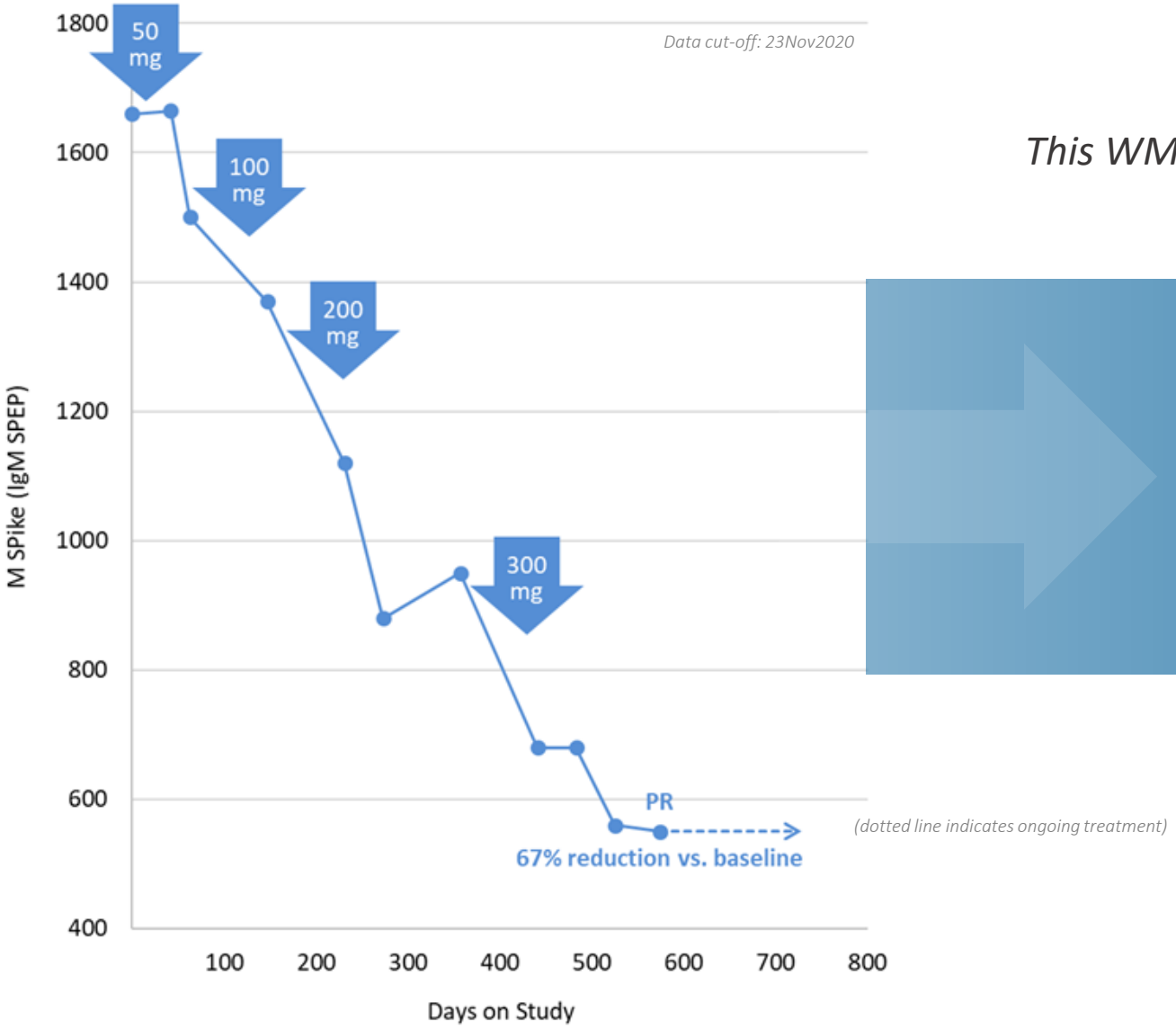
After treating the patient with CA-4948, their tumor no longer expresses NF-κB phospho-p50



(Day 20)

CA-4948 in Lymphoma

Anti-Cancer Activity and Dose Response in a Patient with Waldenströms Macroglobulinemia (WM)



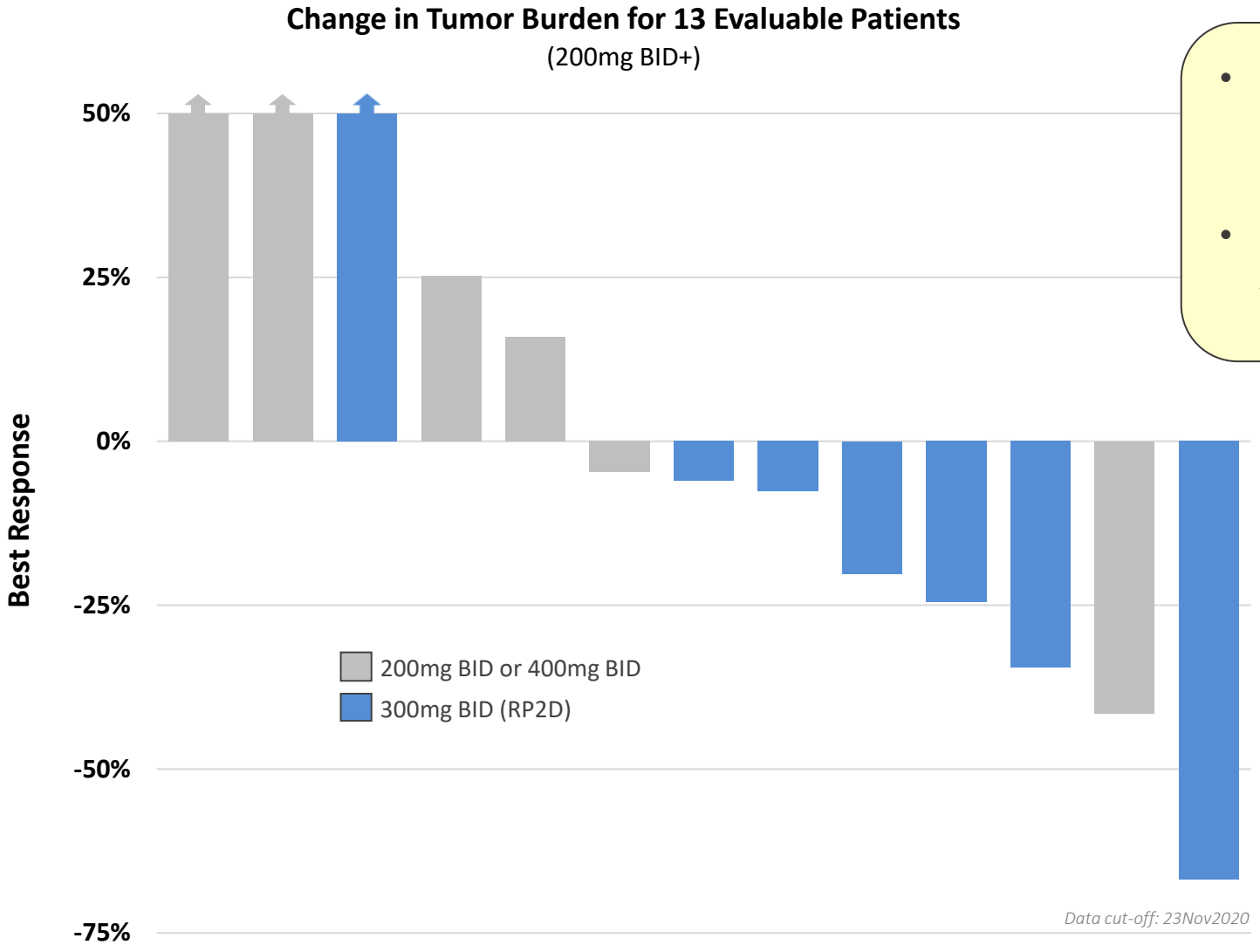
Note:
This WM patient is one of the two patients in the Ph1 study who tested positive for MYD88

Demonstrated Anti-Cancer Activity
Objective Response observed at 300mg BID (RP2D)

Demonstrated Dose Response
Tumor burden decreased with each increase in dose

CA-4948 in Lymphoma

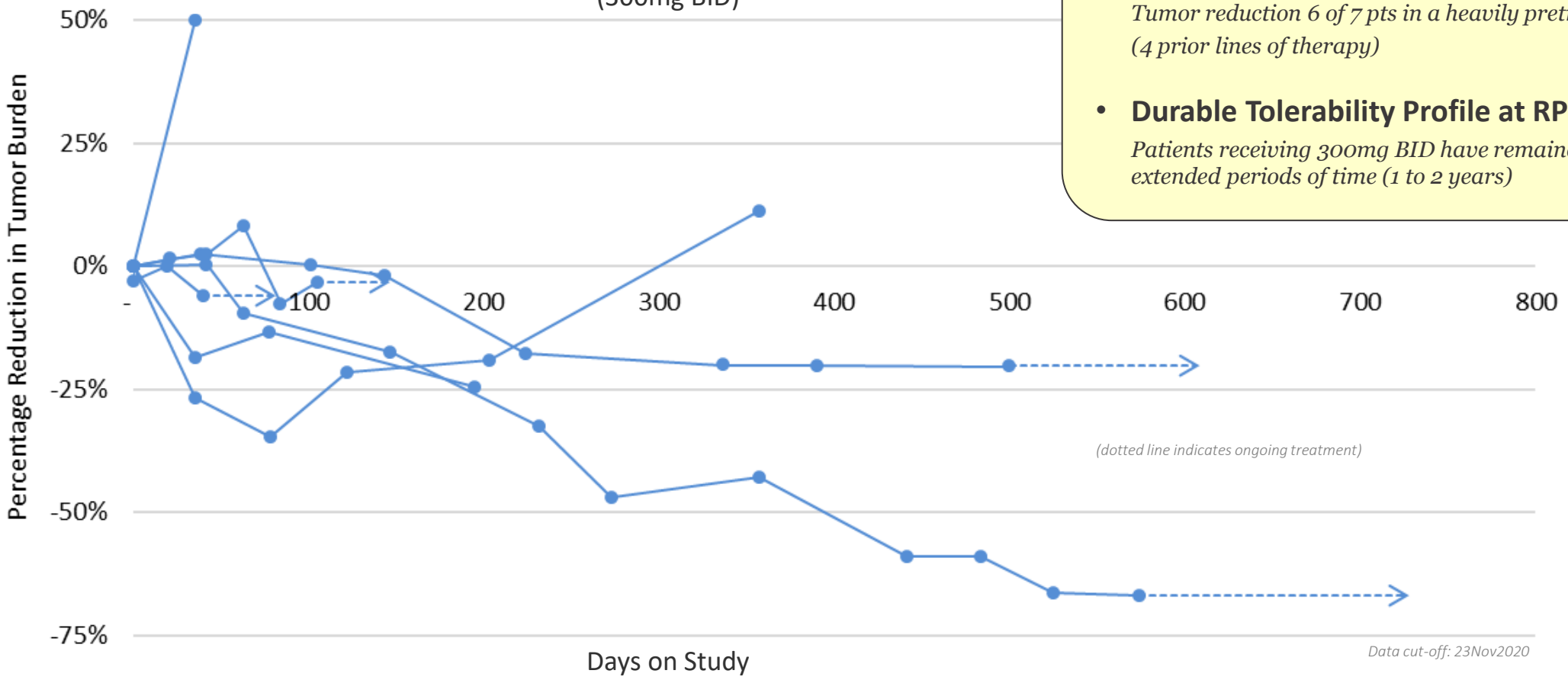
In Updated Ph1 Data, 300mg BID (RP2D) Offered Best Balance of Tolerability and Anti-Cancer Activity



- **Clear Single Agent Anti-Cancer Activity at RP2D**
  Tumor reduction 6 of 7 pts in a heavily pretreated population (4 prior lines of therapy)
- **Durable Tolerability Profile at RP2D**
  Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)

CA-4948 in Lymphoma

In Updated Ph1 Data, 300mg BID (RP2D) Offered Best Balance of Tolerability and Anti-Cancer Activity

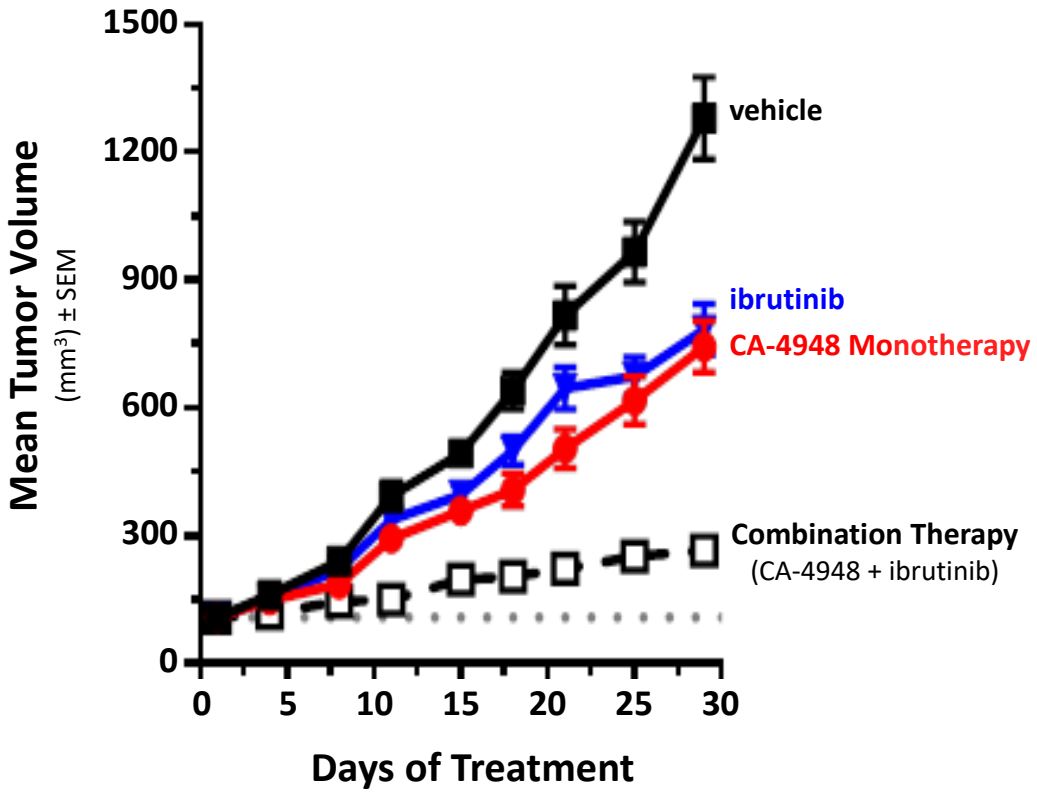


- **Clear Single Agent Anti-Cancer Activity at RP2D**
  Tumor reduction 6 of 7 pts in a heavily pretreated population (4 prior lines of therapy)
- **Durable Tolerability Profile at RP2D**
  Patients receiving 300mg BID have remained on therapy for extended periods of time (1 to 2 years)

CA-4948 in Lymphoma

2021 Plan: Initiate Clinical Study in Combination Therapy (CA-4948 + ibrutinib)

Anti-Cancer Activity
in Monotherapy and Combination Therapy
in MYD88-altered DLBCL preclinical model (OCI-Ly10)



Booher et al. Waldenstrom Roadmap Symposium 2019

Mechanism of Action Supports Combination

- CA-4948 potentially offers a novel mechanism for reducing NF-κB activity by targeting the TLR/myddosome (a parallel/complementary pathway to the BCR/BTK pathway)

Clear Single Agent Anti-Cancer Activity

- Monotherapy anti-cancer activity demonstrated in both preclinical models and initial Ph1 data

Clear Synergy with ibrutinib

- CA-4948 and ibrutinib show clear synergy in preclinical models
- Next Step: initiate clinical study of CA-4948 and ibrutinib

CA-4948 in Lymphoma (combination study)

Trial Design

Study Objectives

Primary: Safety and tolerability of CA-4948 in combination with ibrutinib
Secondary: Pharmacokinetic (PK) profile, preliminary anti-cancer activity

Study Population

- Relapsed/Refractory disease
- Histopathologically confirmed B-cell NHL, including WM/LPL
- Age ≥ 18 years
- ECOG performance Status of ≤ 1

Dosing

- CA-4948 – Oral twice daily
- ibrutinib – Oral daily at labeled dose
- 21-day cycles
- 3+3 escalation design for CA-4948 (1st cohort will be 200mg BID)

Additional Patient Cohorts to be Studied in Planned Expansion

- BTK inhibitor naïve, Marginal Zone Lymphoma (MZL)
- BTK inhibitor naïve, ABC-DLBCL
- BTK inhibitor naïve, Primary CNS Lymphoma (PCNSL)
- Patients with adaptive resistance to ibrutinib

VISTA Targeted Program in Solid Tumors

CI-8993: In development for treatment of cancers driven by VISTA-mediated Immune Suppression

CI-8993 Overview

In Development for VISTA Expressing and Infiltrated Cancers

Profile	
Value Proposition	• First-in-class monoclonal antibody antagonist of VISTA • Composition-of-matter IP extends into 2034
Target Patient Population	• Patients with VISTA-expressing cancers (incl. Mesothelioma, NSCLC, and TNBC) • Patients receiving PD1/PDL1 or CTLA4 antibody therapy (or those who have already received it and have developed resistance to it)
Product Description	• Monoclonal antibody developed by ImmuNext/Janssen in partnership with Randy Noelle's lab at Dartmouth (the co-discoverer of VISTA)

CI-8993 Target Background

VISTA is an Important Checkpoint Regulator

RESEARCH ARTICLE SUMMARY

T CELLS

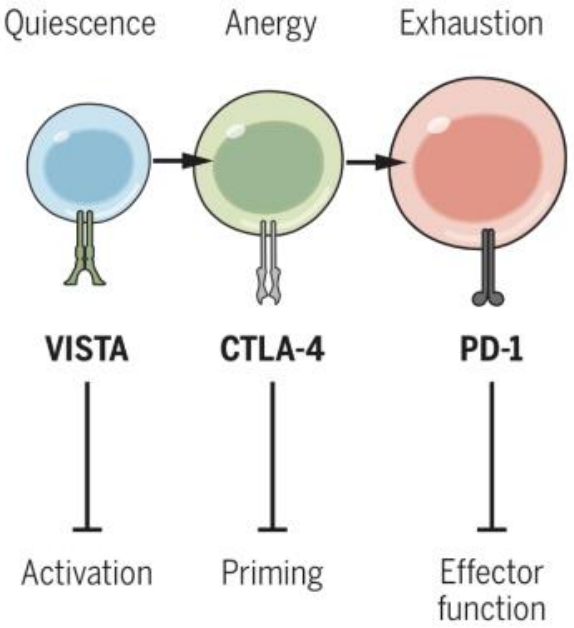
VISTA is a checkpoint regulator for naïve T cell quiescence and peripheral tolerance

Mohamed A. ElTanbouly*, Yanding Zhao*, Elizabeth Nowak, Jiannan Li, Evelien Schaafsma, Isabelle Le Mercier, Sabrina Ceeraz, J. Louise Lines, Changwei Peng, Catherine Carriere, Xin Huang, Maria Day, Brent Koehn, Sam W. Lee, Milagros Silva Morales, Kristin A. Hogquist, Stephen C. Jameson, Daniel Mueller, Jay Rothstein, Bruce R. Blazar, Chao Cheng†, Randolph J. Noelle†

- CTLA-4, PD-1, and VISTA are the three main players in controlling checkpoint blockade
- VISTA controls early T cell activation events
- Blockade of VISTA will allow for an expanded T cell response against tumors

Eltanbouly et al. Science. 2020

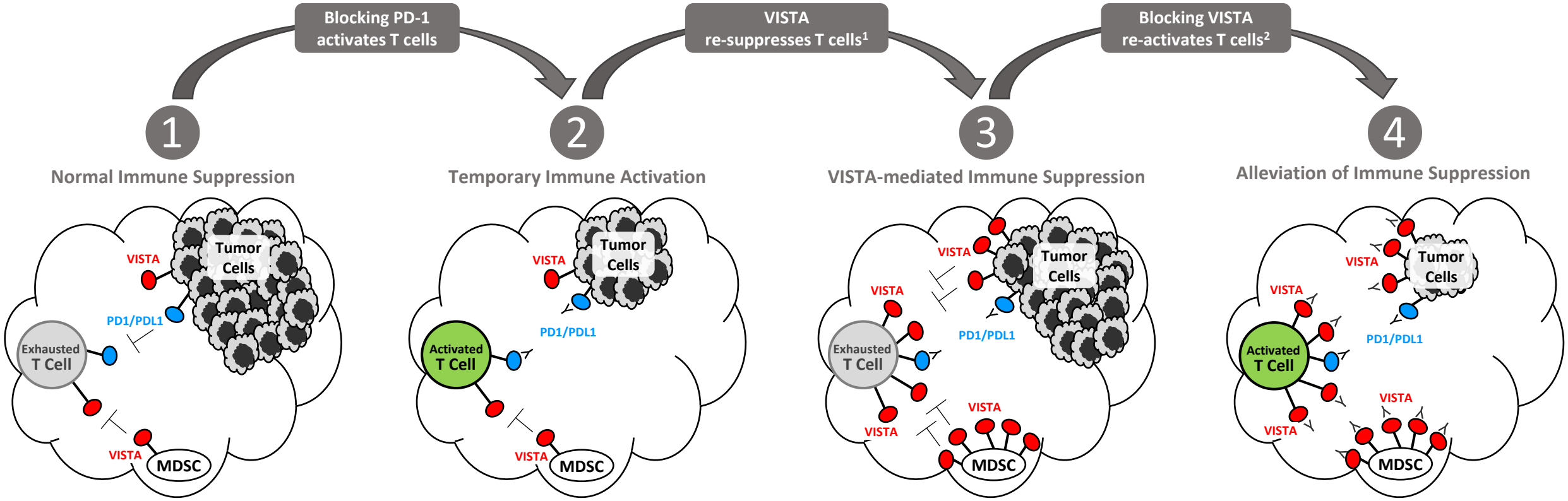
Integration of VISTA with other well-established negative checkpoint regulators of T cell activation



Eltanbouly et al. Science. 2020

CI-8993 Target Background

Role of VISTA in Immune Suppression in the Tumor Microenvironment (TME)



T cells Activated after PD1 Treatment

T cells Suppressed by VISTA after PD1 Treatment

blocking PD1 causes up to 5x increase in VISTA expression[1]

T cells Re-Activated after VISTA Treatment

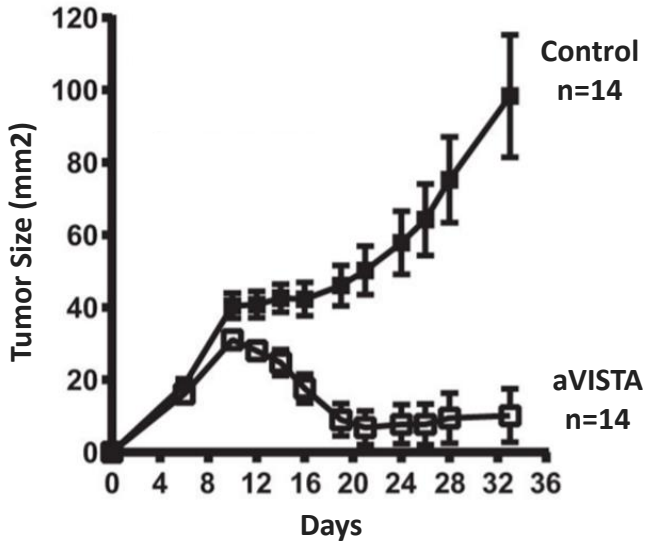
[1] Gao et al. Nature. 2017. 23: 551–555
[2] Data from ImmuNext preclinical studies

CI-8993 Preclinical Data

Preclinical anti-cancer activity demonstrated in both monotherapy & combination therapy

Monotherapy

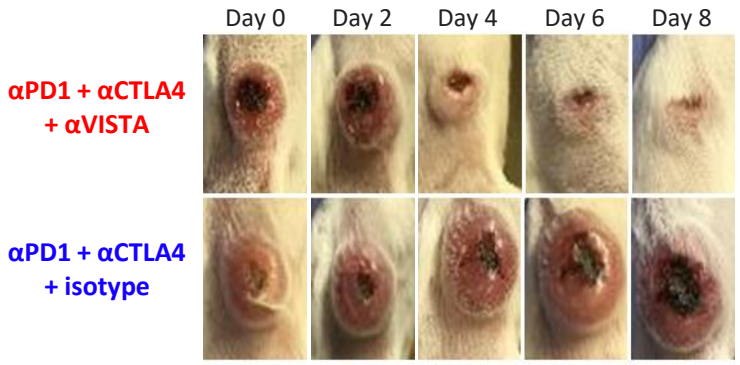
Anti-VISTA inhibited tumor growth in B16ova melanoma model[1]

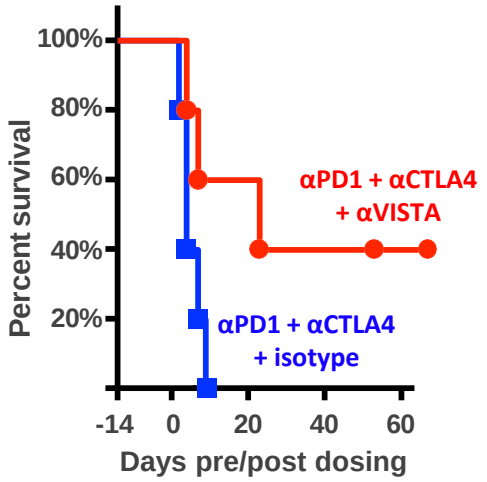


[1] Le Mercier et al. Cancer Res. 2014 Apr 1

Combination Therapy

Anti-VISTA inhibited xenograft growth in checkpoint resistant CT26 model[2]



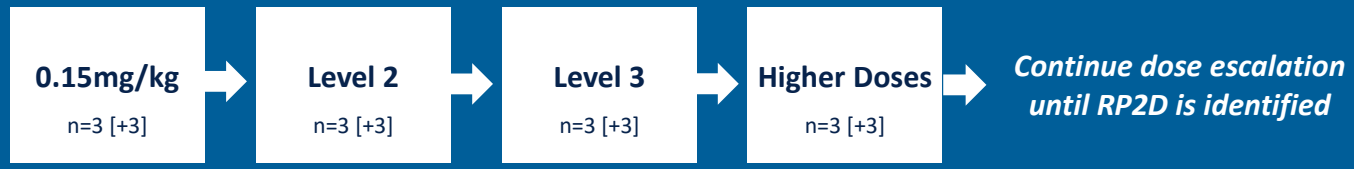


[2] J. Lines, IEBMC Conference 2019

CI-8993 Clinical Plan

Phase 1 dose escalation study design

Curis Design for Ph1 Dose Escalation Study



Patient Population

- Patients with advanced refractory solid tumors (includes mesothelioma, melanoma, NSCLC, TNBC)

Treatment

- Bi-weekly dosing
- Mitigate potential toxicities by desensitization, premedication, dosing interval and duration

Objective

- Safety, PK/PD, tolerability during dose escalation
- Anti-cancer activity during expansion

Prior clinical development of CI-8993:

CI-8993 was originally developed by Janssen (JNJ-61610588)

- JNJ licensed VISTA IP from ImmuNext in 2012 and initiated a Ph1 study in 2016
- 12 patients were enrolled; initial dose level was 0.005mg/kg
- Low-grade transient Cytokine Release Syndrome (CRS) seen at 0.15mg/kg and above

JNJ halted study after 1 DLT at sub-therapeutic dose level

- The only patient treated at 0.3mg/kg experienced grade 3 CRS-associated encephalopathy after 36hrs on treatment
- Patient was initially treated w/antibiotics; symptoms resolved after treatment with tocilizumab
- JNJ opted to halt the study and return IP to ImmuNext

Target range for expected anti-cancer activity (0.5 – 2.0mg/kg) was never reached

Curis Design for Ph1 Study Design Incorporates Key Learnings from Janssen Ph1 Study

- CRS is likely an on-target toxicity; indicates drug is hitting the target and inducing inflammatory response
- Oncology community is now familiar with managing CRS; NCCN guidelines were issued in 2018
- FDA cleared the study IND which outlined our plan for managing CRS and enabling escalation to therapeutic dose levels

Company

Summary

Investment Thesis	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need
Robust Pipeline	CA-4948: first-in-class inhibitor of IRAK4 in oncology *There are no drugs currently approved for IRAK4 inhibition in oncology* CI-8993: first-in-class antagonist of VISTA *There are no drugs currently approved for VISTA inhibition*
Potential Catalysts	✓ 1H 2021: Initiate combination study of CA-4948 and ibrutinib in NHL patients ✓ Mid 2021: Report expanded data in CA-4948 Ph1 study in AML/MDS patients 2H 2021: Report initial data in CI-8993 dose escalation Ph1 study

Curis

Leadership Team

Rachel Blasbalg
Head, Human Resources

James Dentzer
President & CEO

Christine Guertin
Head, Regulatory

Robert Martell
Head, R&D

Mark Noel
Head, Intellectual Property

Reinhard von Roemeling
Head, Clinical Development

Raul Soikes
Head, Portfolio Management

Nancy Soohoo
General Counsel

William Steinkrauss
Chief Financial Officer

End of Corporate Presentation

NASDAQ: CRIS