

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 forwardlooking 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.

Corporate Overview



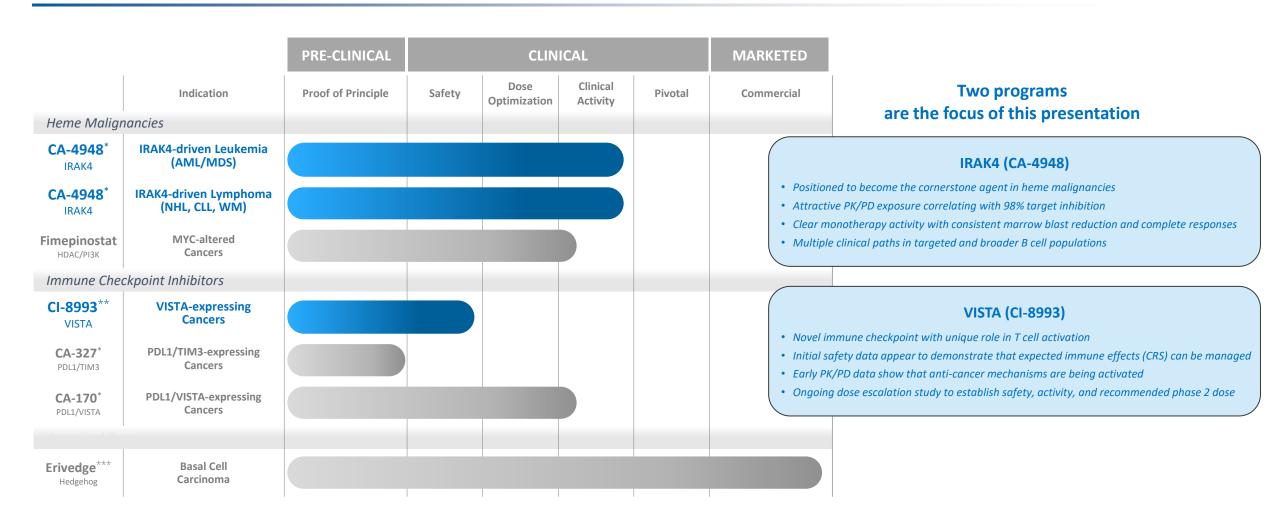
Summary

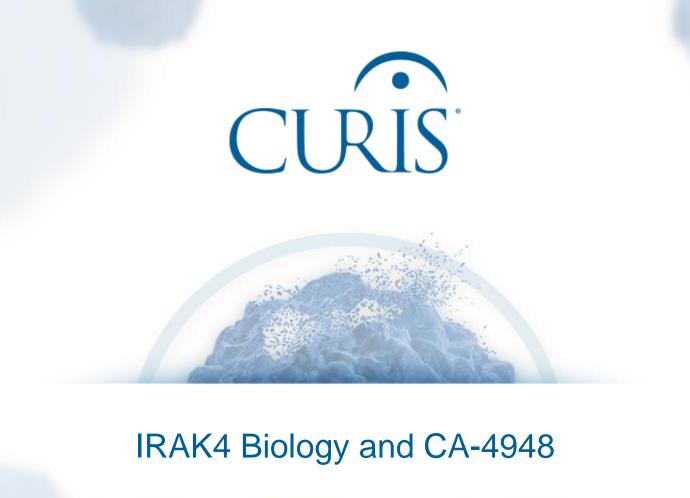
Investment Thesis	Curis seeks to develop novel, first-in-class, cancer therapeutics that we believe have significant potential in areas of unmet patient need Cash and investments of approximately \$150M as of September 30, 2021; cash runway into 2024
Robust Pipeline	CA-4948: first-in-class inhibitor 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
Upcoming Milestones	 1H 2022: Discuss potential for rapid approval path for CA-4948 with FDA 1H 2022: Report initial data for CA-4948 in combination with ibrutinib in NHL 2022: Report updated data for CA-4948 in AML/MDS monotherapy 2H 2022: Report initial efficacy data for CI-8993 (VISTA) 2H 2022: Report initial data for CA-4948 in combination with aza or ven in AML/MDS

Pipeline



Curis develops novel, first-in-class cancer drugs





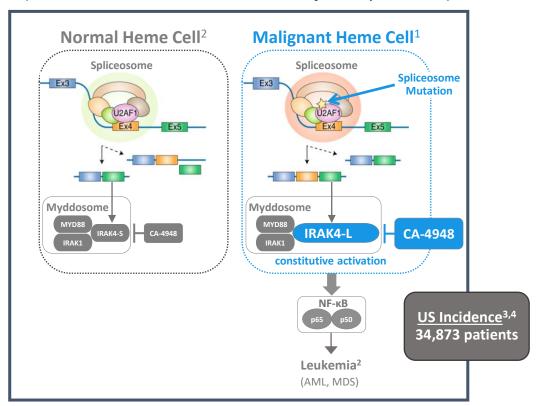
IRAK4 Biology and CA-4948



IRAK4 is a novel and important target across multiple heme malignancies

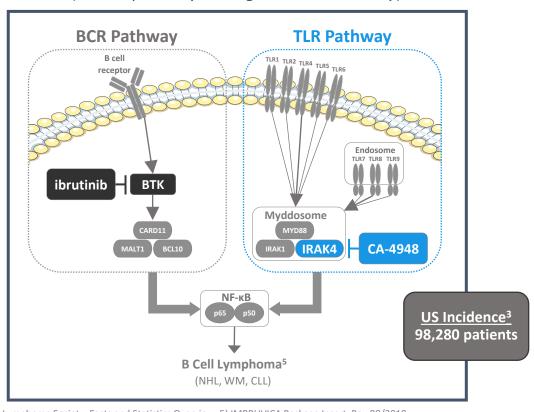
IRAK4 in AML/MDS

Spliceosome mutation drives overexpression of IRAK4-L (which causes constitutive activation of the myddosome)



IRAK4 in B Cell Cancers

TLR Pathway is dependent upon IRAK4 for function (the 2nd pathway driving NF-кВ overactivity)

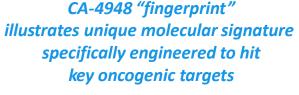


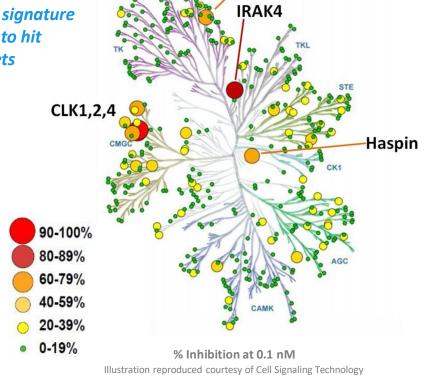
¹⁾ Guillamot et al. Nat Cell Biol 2019; 2) Smith et al. Nat Cell Biol 2019; 3) American Cancer Society, Cancer Facts & Figures 2020; 4) Leukemia & Lymphoma Society, Facts and Statistics Overview; 5) IMBRUVICA Package Insert. Rev 08/2018

CA-4948 is the Leading IRAK4 Inhibitor in Development for Cancer

Targeted design offers added potential benefit of also hitting FLT3

CA-4948 Kinase Interaction Map





CA-4948 Binding Affinity

	Target	K _d nM	
	IRAK1	12,000	
	IRAK2	>20,000	
	IRAK3	8,500	
	IRAK4	23	
	DYRK1A	25	
	FLT3 wt	31	
	FLT3 (D835H)	5	
	FLT3 (D835V)	44	
	FLT3 (D835Y)	3	
	FLT3 (ITD)	8	
	FLT3 (K663Q)	47	
	FLT3 (N841I)	16	
	Haspin (GSG2)	32	
	CLK1	10	
	CLK2	20	
	CLK3	>20,000	
	CLK4	14	
	TrkA	130	

DiscoverX Kinase Panel (378 kinases screened)



CA-4948 binds specifically and with high affinity to IRAK4

Dual targeting of IRAK4 and FLT3 confers a potential efficacy advantage vs. other IRAK4 inhibitors and expands potential to additional genetic populations

CA-4948 PK/PD



Attractive PK profile supports BID dosing and high target suppression

Trough

Exposure

2.5µM

4.1µM

Dose

200mg

300mg

Inhibition

97% **98%**

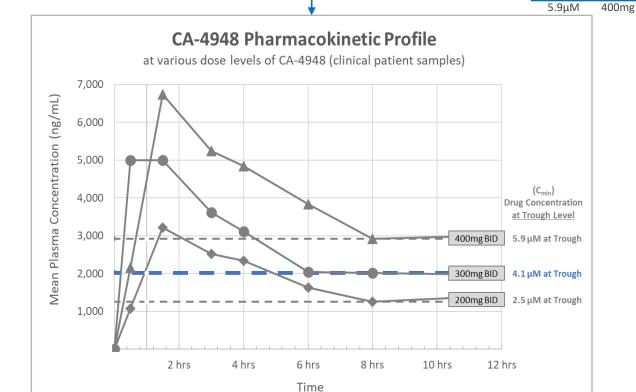
98%

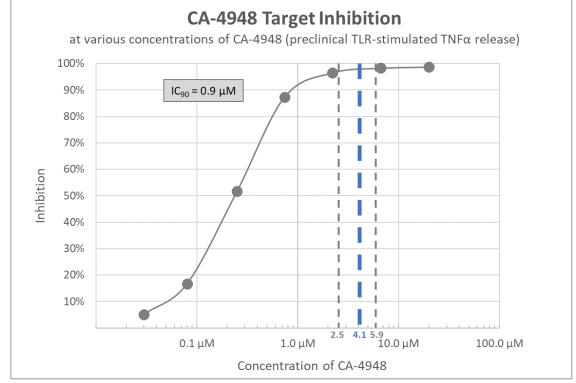
Attractive PK Profile

- Half-life of ~6 hours
- Supports BID dosing regimen

High Target Suppression

Exposure at RP2D correlates with 98% inhibition





Data from CA-4948 lymphoma clinical study

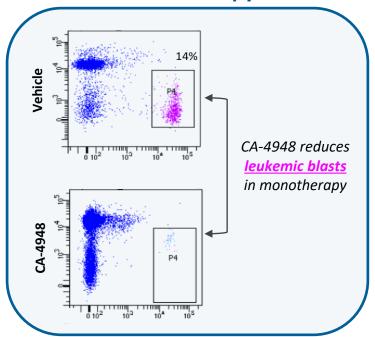
Data from preclinical study of target inhibition

CA-4948 Preclinical Data



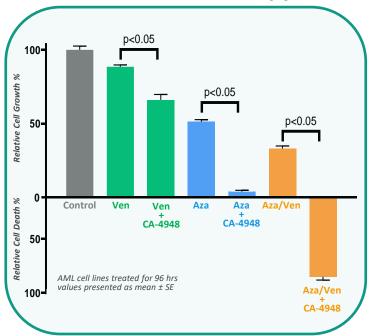
Clear anti-cancer activity suggests broad potential across heme malignancies

AML/MDS Monotherapy



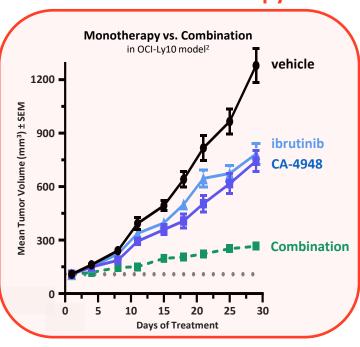
CA-4948 demonstrates monotherapy activity in patient-derived xenografts¹

AML/MDS Combination Therapy



CA-4948 demonstrates synergy with both azacitidine and venetoclax in THP-1 model²

B Cell Cancers Combination Therapy



CA-4948 demonstrates synergy with Ibrutinib in OCI-Ly10 model³

¹⁾ Choudhary et al. AACR 2017; 2) Curis AML MDS poster, EHA 2021; 3) Booher et al. Waldenström Roadmap Symposium 2019

CA-4948 Clinical Plan



Ongoing clinical studies in AML/MDS and B cell cancers

AML/MDS Monotherapy

(relapsed/refractory)

Patients with Targeted Mutation

- Patients with spliceosome mutation
- Patients with FLT3 mutation

Supports rapid regulatory path

- Spliceosome mutation is a leading cause of IRAK4-L overexpression¹
- Signaling through IRAK4 is an adaptive response mechanism for FLT3 patients treated with a FLT3 inhibitor²

AML/MDS Combination Therapy

(relapsed/refractory)

Patients without Targeted Mutation

- HMA-naïve, CA-4948 + HMA
- Venetoclax naïve, CA-4948 + venetoclax

Supports use in broad population

- Clinical data show CA-4948 reduces tumor burden in the significant majority of evaluable patients
- Preclinical data demonstrate synergy with azacitidine and venetoclax

B Cell Cancers Combination Therapy

(relapsed/refractory)

Patients with IRAK4 Pathway activation

- BTKi-naïve, Marginal Zone Lymphoma
- BTKi-naïve, Primary CNS Lymphoma
- BTKi-naïve, ABC-DLBCL
- Patients (any tumor type) who have relapsed after adaptive resistance to ibrutinib

Maximizes speed and probability of success

- Marginal Zone Lymphoma, Primary CNS Lymphoma, and ABC-DLBCL are aggressive indications associated with TLR/IRAK4 Pathway activity
- If patients who relapsed on ibrutinib can get clinical response with combination, it is likely impact of adding CA-4948



CA-4948 in AML/MDS

CA-4948 in AML/MDS



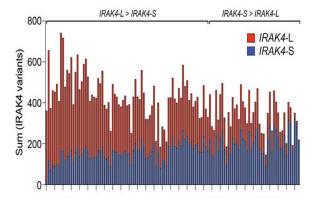
Clinical studies designed to leverage the role of IRAK4/FLT3 in AML/MDS

% of Patient <u>Disease Driver</u> <u>Population</u>

IRAK4-L	> 50%1
FLT3	25-30% ²
TET2	10-20%3
IDH2	9-13%4
IDH1	6-10%4
CEBPA	~10%3

Rationale for Monotherapy

- IRAK4 / FLT3 is the largest targeted market in AML/MDS^{1,2}
- Spliceosome mutation is a leading cause of IRAK4-L overexpression¹
- Signaling through IRAK4 is an adaptive response mechanism for FLT3 patients treated with a FLT3 inhibitor⁵



Rationale for Combination

- Nearly all patients express some level of IRAK4-L¹
- Clinical data show CA-4948 reduces tumor burden in the significant majority of evaluable patients
- Preclinical data demonstrate clear synergy with azacitidine and venetoclax
 - O IRAK4 stimulates NF-κB and ultimately an array of anti-apoptotic factors (beyond BCL2), which prevent the effectiveness of anti-leukemic drugs
 - Blocking this effect with CA-4948 synergistically enhances the anti-cancer efficacy of those agents in preclinical models

- 1) Smith et al. Nat Cell Biol 2019
- 2) Saygin, et al. J Hematol Oncol. 2017 Apr 18
- 3) DiNardo, Cortes. Hematology Am Soc Hematol Educ Program. 2016

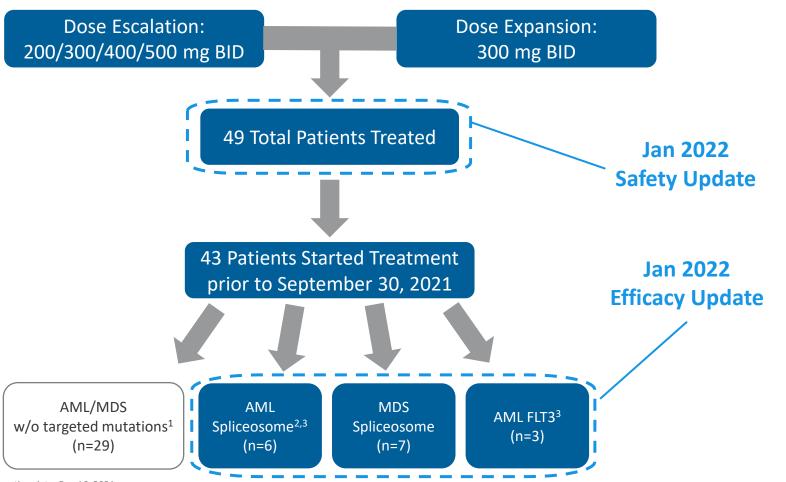
AML patients (ordered by ratio of IRAK4-L to IRAK4-S)

- 4) DiNardo et al. N Engl J Med 2018
- 5) Rabik et al. Ann Transl Med 2020

CA-4948 in AML and MDS



Open-label, single arm, Phase 1/2 dose escalation and expansion study



Study Objectives

- 1°: Determine maximum tolerated dose
 Determine recommended Phase 2 dose
- 2°: Pharmacokinetic (PK) profile Preliminary anti-cancer activity

Study Population

- Relapsed/Refractory AML or high-risk MDS
- ECOG performance Status of ≤ 2
- Age ≥ 18 years

Dosing

- Oral, Twice Daily (BID) Dosing
- 28-day cycles

Data extraction date: Dec 16, 2021

^{1.} These are non-targeted patients, due to lack of Spliceosome or FLT3 mutation, this population will be addressed in the combination therapy study; 2. One patient was not response evaluable because of discontinuation due to patient decision;

^{3.} Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation)

Well-Tolerated and Manageable AE Profile for CA-4948 in AML/MDS with No Cumulative Toxicities Observed



No Grade 4 or 5 TRAEs reported; all AEs were manageable

Recommended Phase 2 Dose

Grade 3+ Treatment-Related Adverse Event		0 mg BID (N = 3)		mg BID N = 26)) mg BID N = 17)		0 mg BID (N = 3)
		n (%)		n (%)		n (%)		n (%)
Number of patients having grade 3+ treatment-related AEs	1	(33.3)	6	(23.1)	6	(35.3)	2	(66.7)
Alanine aminotransferase increased	1	(33.3)	0		0		0	
Blood creatine phosphokinase increased	0		1	(3.8)	0		0	
Dizziness	1	(33.3)	0		0		0	
Dyspnoea	0		0		1	(5.9)	0	
Enterobacter infection	0		0		1	(5.9)	0	
Fatigue	0		0		1	(5.9)	0	
Gastrointestinal haemorrhage	0		1	(3.8)	0		0	
Hypophosphataemia	0		1	(3.8)	0		0	
Hypotension	0		1	(3.8)	0		0	
Lipase increased	0		2	(7.7)	0		0	
Platelet count decreased	0		1	(3.8)	0		0	
Presyncope	0		0		1	(5.9)	0	
Rhabdomyolysis	0		1	(3.8)	2	(11.8)	1	(33.3)
Syncope	0		0	,	0		1	(33.3)
				•				

Well-tolerated and manageable AE profile with no cumulative toxicities reported

Data extraction date: Dec 16, 2021

No dose-limiting myelosuppression reported, which is a life-threatening problem characteristic of many cancer treatments, making CA-4948 favorable for combinations

^{1.} Data for the two patients that have escalated from 300 mg BID to 400 mg BID were included in the 400 mg BID dose group

Encouraging Clinical Activity in R/R AML/MDS Patient Populations



CA-4948 shows activity as a monotherapy in patients with Spliceosome and FLT3 mutations

Best Response	Efficacy
Population #1: AML Spliceosome Patients ¹	
CR/CRh Rate	2/5 (40%)
CR	1/5 (20%)
CRh	1/5 (20%)
Population #2: MDS Spliceosome Patients	
Objective Response Rate (ORR)	4/7 (57%)
CR	0/7 (0%)
mCR	4/7 (57%)
Population #3: AML FLT3 Patients ¹	
CR/CRh Rate	1/3 (33%)
CR	1/3 (33%)
CRh	0/3 (0%)

The CR and CRh patients are both MRD-negative

1 mCR patient went to Stem Cell Transplant (SCT)

FLT3 mutation eradicated in 2 out of 3 patients

Data extraction date: Dec 16, 2021.

1. Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

Response criteria per 2017 ELN Criteria for AML and Modified IWG Criteria for MDS:

CR = Complete Remission

CRh = CR with partial hematologic recovery

mCR = marrow CR





Clinical Data: R/R AML Patients with Spliceosome Mutation

Patient Population #1

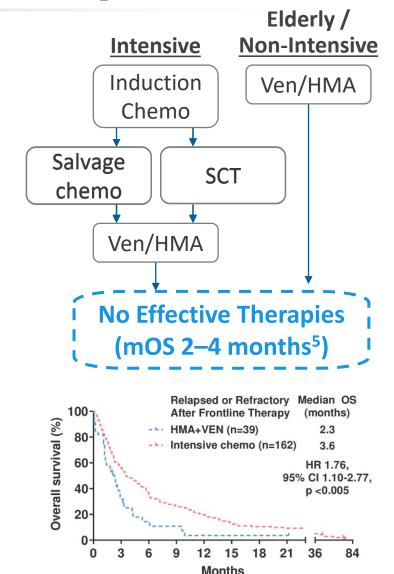
Unmet Need for R/R AML Patients with Spliceosome Mutation



No approved targeted therapies and no unified standard of care for these patients

- Spliceosome mutations occur in ~10% of AML patients¹
 - These mutations create a chronic inflammatory marrow microenvironment², which impairs hematologic recovery³
 - Ability to achieve CR is impaired in patients with U2AF1/SF3B1 mutation⁴
- There are no effective therapies for patients R/R to Ven/HMA: no unified standard of care

Opportunity to meaningfully improve outcomes in R/R AML patients with spliceosome mutations



^{1.} DiNardo et al, Hematology Am Soc 2016; 2. Smith et al. Nat Cell Biol 2019; 3. Trowbridge JEM 2021. Ochi Cancers 2021. Hou, Oncotarget 2016; 4. Hou, Oncotarget 2016; 5. Maiti et al. Haemtologica 2021

Initial CA-4948 Data Compare Favorably to Existing Therapies



Potential to meaningfully improve outcomes in R/R AML patients with spliceosome mutation

Most Commonly Used in R/R AML with Wild Type FLT3/IDH1

CA-4948	Decitabine ^{2,3}	Azacitidine ^{2,4}	LoDAC ⁵	Gemtuzumab Ozogamicin ^{2,6}
IRAK4 Inhibitor	НМА	НМА	Chemotherapy	Monoclonal Anti-CD33 Antibody (ADC)
• 40% CR/CRh rate (2 of 5 patients)	• ~16% CR rate	• 17% CR/CRi rate	• ~13% ORR	• ~26% CR
No dose-limiting myelosuppression	Myelosuppressive	Myelosuppressive	Myelosuppressive and Black Box Warning	Myelosuppressive and Black Box Warning
Oral Administration	IV Administration	IV or SC Administration	IV Administration	IV Administration

>6 months on CA-4948 for patients with CR/CRh

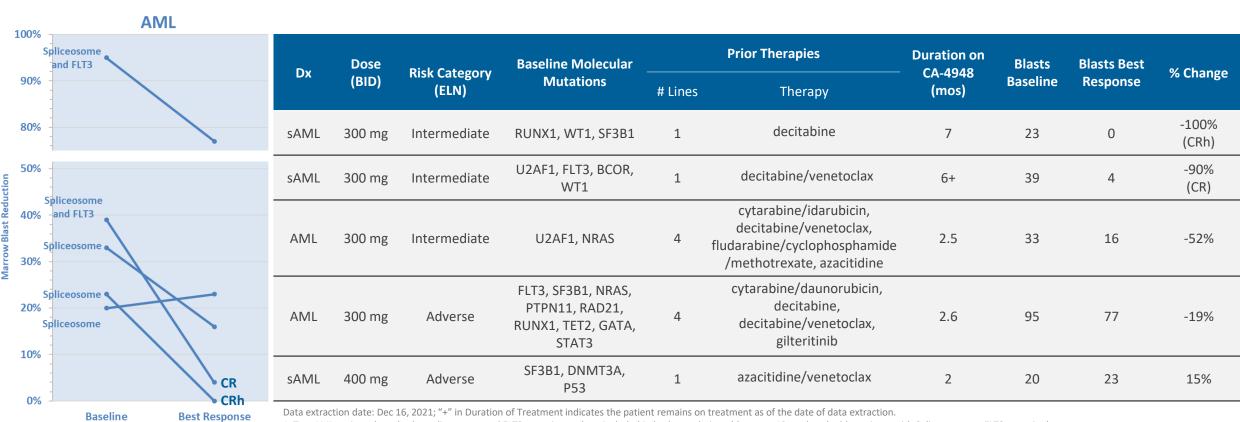
Initial CA-4948 data compare favorably vs. historical responses with mainstay treatments for R/R AML patients with wild type FLT3/IDH

^{1.} CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Excludes Investigational Therapies; 2. Product Package Insert; 3. Ritchie et al, Leuk Lymphoma 2013; 4. Itzykson et al, Leuk Res 2014; 5. Frikha et al, Bulletin du Cancer 1996; 6. Gemtuzumab ozogamicin is only approved for patients with newly-diagnosed CD33-positive AML or R/R CD33-positive AML

Encouraging Clinical Activity in R/R AML Patients with Spliceosome Mutation



Achieved 40% CR/CRh rate, with treatment duration >6 months to date in responding patients



^{1.} Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

CA-4948 achieved CR/CRh responses, despite transformed AML being historically highly resistant to treatment





Clinical Data: R/R MDS Patients with Spliceosome Mutation

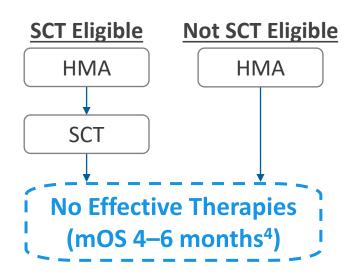
Patient Population #2

Spliceosome Mutations Common in MDS



Large unmet need for R/R MDS patients with spliceosome mutation

- Spliceosome mutations (U2AF1/SF3B1) are the most prominent mutations in MDS, accounting for ~30% of all MDS patients¹
 - These mutations create a chronic inflammatory marrow microenvironment², which impairs hematologic recovery³
- There are no effective therapies for patients R/R to HMA: chemotherapy is standard of care



Current standard of care offers limited therapeutic benefit to patients

Clear Unmet Need in Relapsed/Refractory MDS



Current standard of care offers little therapeutic benefit to patients

Most Commonly Used Therapies in R/R MDS¹

CA-4948	Chemotherapy ²	Decitabine ³	Azacitidine ³
IRAK4 Inhibitor	Chemotherapy	НМА	НМА
• 57% mCR rate (4 of 7 patients, incl. 1 that went to SCT)	• ~8% ORR	2 nd line response data unavailable	• 2 nd line response data unavailable
No dose-limiting myelosuppression	Myelosuppressive and Black Box Warning	Myelosuppressive	Myelosuppressive
Oral Administration	IV Administration	IV Administration	IV or SC Administration

In MDS post-HMA mOS is 4–6 months⁴; clear unmet need for these patients

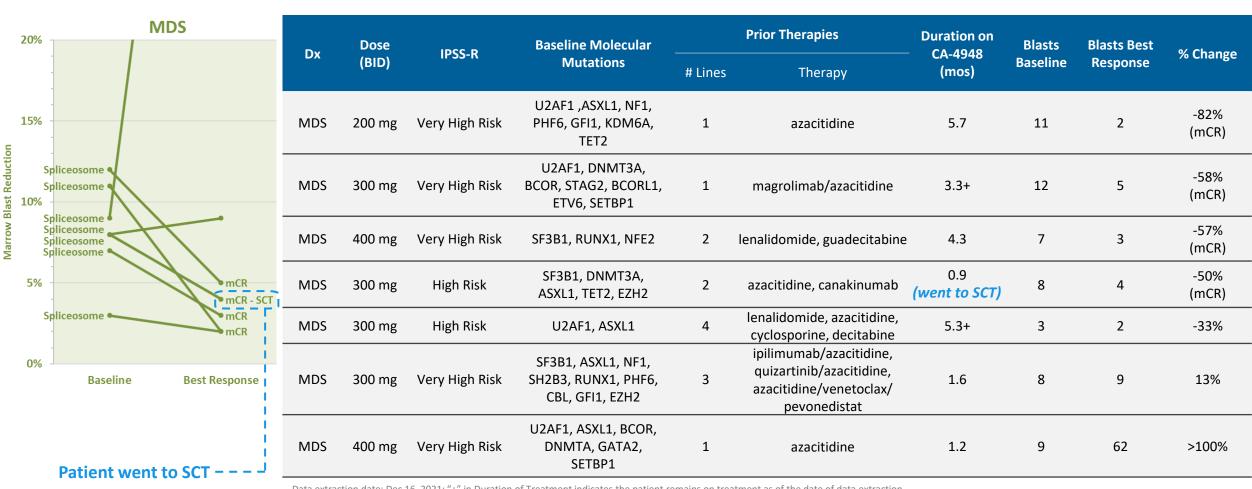
Initial CA-4948 data compared favorably vs. historical responses with the mainstay treatment for R/R MDS patients

^{1.} CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Excludes Investigational Therapies; 2. Prébet et al., JCO 2011; 3. Product Package Insert.; 4. Jabbour et al Cancer 2010; Prébet et al., JCO 2011; Duong et al, Clin Lymphoma Myeloma Leuk, 2013.

Encouraging Clinical Activity in R/R MDS Patients with Spliceosome Mutation CLRIS



Marrow blast reduction achieved in 5 of 7 patients, including 4 marrow CRs



Data extraction date: Dec 16, 2021; "+" in Duration of Treatment indicates the patient remains on treatment as of the date of data extraction

Consistent tumor burden reduction in targeted population with limited options





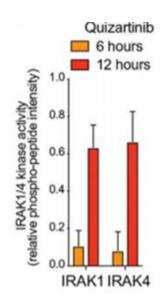
Clinical Data: R/R AML Patients with FLT3 Mutation

Patient Population #3

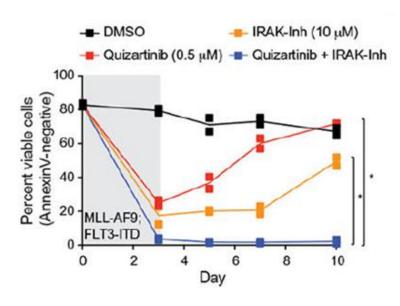
IRAK4 Signaling Drives Resistance to FLT3 Inhibitors



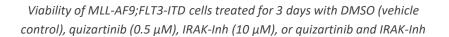
IRAK4 inhibition is synergistic with, and prevents adaptive resistance to, FLT3 inhibition

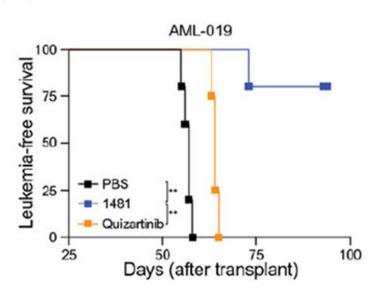


- IRAK4 activity increases after quizartinib treatment of MLL-AF9 FLT3-ITD cells
- IRAK4 activity also shown to increase in patients during gilteritinib treatment



IRAK and FLT3 inhibition is synergistically cytotoxic





Mice die if treated with quizartinib, but survive if treated with IRAK/FLT3 inhibitor (1481)

Leukemia-free survival of NRGS mice xenografted with AML-019

CA-4948 May Address Unmet Need in R/R AML Patients with FLT3 Mutation



No approved therapies for patients R/R to FLT3 inhibitors

Most Commonly Used Therapies in R/R AML Patients with FLT3 Mutation¹

CA-4948	Gilteritinib ^{2,3}	Azacitidine ²	Decitabine ²	Gemtuzumab Ozogamicin ^{2,4}
IRAK4 Inhibitor	FLT3 Inhibitor	НМА	НМА	Monoclonal Anti-CD33 Antibody (ADC)
• 33% CR (1 of 3 patients)	• ~12% CR	2 nd line response data unavailable	2 nd line response data unavailable	• ~26% CR
No dose-limiting myelosuppression	No dose-limiting myelosuppression	Myelosuppressive	Myelosuppressive	Myelosuppressive and Black Box Warning
Oral Administration	Oral Administration	IV or SC Administration	IV Administration	IV Administration

~30% of AML patients have FLT3 mutation⁵

Dual inhibition of IRAK4 and FLT3 may lead to increased efficacy, as signaling through IRAK4 drives resistance to FLT3 inhibitors⁶

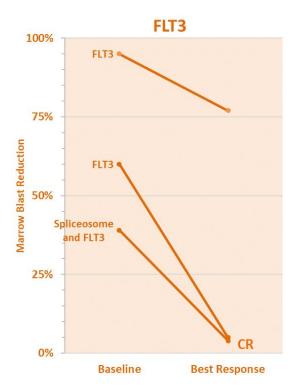
IRAK4/FLT3 inhibition may improve efficacy in R/R AML patients with FLT3 mutation⁵

^{1.} CancerMPact Treatment Architecture U.S. AML, Cerner Enviza, www.cancermpact.com, accessed January 3, 2022. Excludes Investigational Therapies; 2. Product Package Insert; 3. Perl et al NEJM 2019; 4. Gemtuzumab ozogamicin is only approved for patients with CD33-positive AML; 5. Saygin, et al. J Hematol Oncol. 2017; 6. Melgar, Sci Transl Med. 2019

Encouraging Clinical Activity in R/R AML Patients with FLT3 Mutation



Achieving disease modification in heavily pretreated patients with CA-4948 monotherapy



Dir	Dose	Risk	Baseline Molecular		Prior Therapies	Duration on	Blasts	Blasts Best	0/ Change
Dx	(BID)	Category (ELN)	Mutations	# Lines	Therapy	CA-4948 (mos)	Baseline	Response	% Change
AML	400 mg	Adverse	FLT3 (eradicated at C3D1), ASXL1, BCOR, CEBPA (eradicated at C3D1), CSF3R, EZH2, NRAS, RUNX1 (X3), STAG2, TET2(X2,1) (eradicated at C3D1)	2	decitabine/venetoclax, gilteritinib (refractory to gilteritinib)	5.1	60	5	-92%
sAML	300 mg	Intermediate	FLT3 (eradicated at C4D1), BCOR (eradicated at C4D1), U2AF1 (decreased to 1.3 VAF at C4D1), WT1 (eradicated at C4D1)	1	decitabine/venetoclax	6.2+	39	4	-90% (CR)
AML	300 mg	Adverse	FLT3, SF3B1, NRAS, PTPN11, RAD21, RUNX1, TET2, GATA, STAT3	4	cytarabine/daunorubicin, decitabine/PCM-075, decitabine/venetoclax, gilteritinib	2.6	95	77	-19%

Data extraction date: Dec 16, 2021; "+" in Duration of Treatment indicates the patient remains on treatment as of the date of data extraction.

Significant marrow blast reduction and FLT3 mutation eradicated in 2 out of 3 patients

^{1.} Two AML patients have both a spliceosome and FLT3 mutation and are included in both populations (there are 13 total evaluable patients with Spliceosome or FLT3 mutation).

CA-4948 Has Potential to Address Clear Unmet Need in AML and MDS



First-in-class IRAK4 inhibitor targets specific genetic populations in AML and MDS

CA-4948 addresses a novel target (IRAK4) and:

- (1) demonstrates clear anti-cancer activity as an oral single agent
- (2) is active in genetically-defined populations that can be identified and enrolled
- (3) has the added potential benefit of also hitting FLT3
- Well-tolerated and manageable safety profile may provide advantage to existing standard of care therapies as a single agent, and also suggests CA-4948 may be a favorable candidate for addition to combination therapy regimens
- Dual targeting of IRAK4 and FLT3 may prevent adaptive resistance to current FLT3 inhibitors¹
- AML/MDS patients who do not have a spliceosome or FLT3 mutation will be addressed in our combination therapy study

Next Steps in Expansion

- Monotherapy: Spliceosome mutation
- Monotherapy: FLT3 mutation
- Combination: CA-4948 + azacitidine
- Combination: CA-4948 + venetoclax

Plan to discuss potential for a rapid registrational path with FDA in 1H 2022



CA-4948 in B Cell Cancers

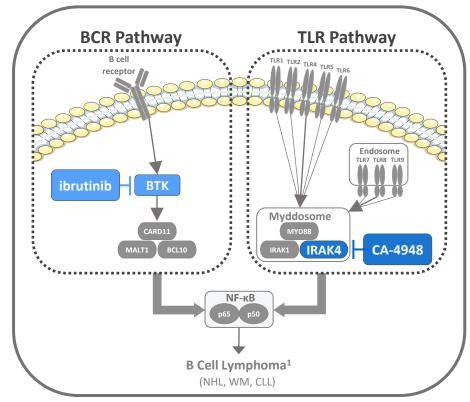
CA-4948 in B Cell Cancers



Combination therapy provides complimentary inhibition of two pathways that drive NF-κΒ

Two Pathways Drive B Cell Cancers

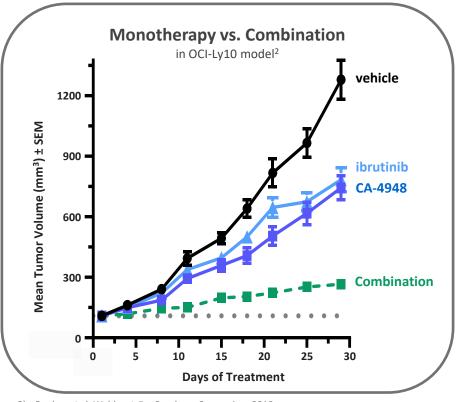
BCR and TLR Pathways independently drive NF-κB overactivity (and NF-κB drives B Cell Cancers)



1) IMBRUVICA Package Insert. Rev 08/2018

Clinical Strategy: Use Combination Therapy

In preclinical testing, blocking both IRAK4 and BTK drove tumor reduction better than blocking either one alone



²⁾ Booher et al. Waldenström Roadmap Symposium 2019

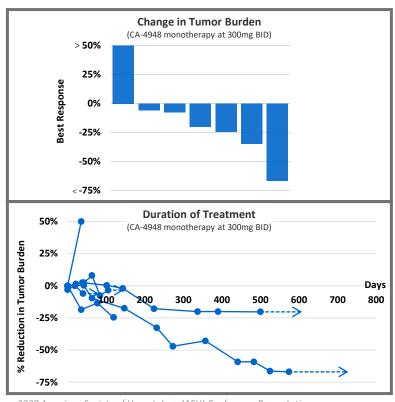
CA-4948 in B Cell Cancers



Proof-of-Concept demonstrated with monotherapy; Combination therapy study in progress

Monotherapy

Ph1 proof-of-concept study demonstrated durable tumor reduction in monotherapy



2020 American Society of Hematology (ASH) Conference Presentation

Combination Therapy

Blocking both IRAK4 and BTK may be better than blocking either one alone

4 Targeted Patient Populations

- BTKi naïve, Marginal Zone Lymphoma
- BTKi naïve, Primary CNS Lymphoma
- BTKi naïve, ABC-DLBCL
- Patients (any tumor type) who have relapsed after adaptive resistance to ibrutinib

Clinical Study in Progress

initial data coming in 1H 2022

CA-4948 in B Cell Cancers



CA-4948 is the ideal candidate to combine with BTKi to maximize downregulation of NF-κB

- Patients are treated with BTKi because downregulating
 NF-κB activity reduces tumor burden in B Cell Cancers
- Two pathways drive NF-κB:
 - 1) BCR Pathway: addressed by blocking BTK
 - 2) TLR Pathway: addressed by blocking IRAK4
- Ph1 clinical data in monotherapy demonstrated proof-ofconcept with clear reduction in tumor burden
- Ph1 clinical data in combination therapy coming in 2022

Next Steps: Combination Therapy

- BTKi naïve, Marginal Zone Lymphoma
- BTKi naïve, Primary CNS Lymphoma
- BTKi naïve, ABC-DLBCL
- Patients (any tumor type) who have relapsed after adaptive resistance to ibrutinib

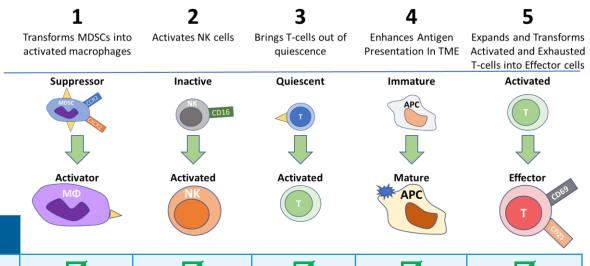
Initial Clinical Data in Combination Therapy to report out in 2022



Anti-cancer Mechanisms of Checkpoint Inhibitors



Role of VISTA may go beyond other checkpoint inhibitors



We believe VISTA inhibition has potential for broad application in many tumor types in monotherapy and in combination with existing checkpoint inhibitors

<u>Checkpoint Inhibitors Approved in Multiple Malignancies:</u>

- Melanoma
- Lung Carcinoma
- Renal Cell Carcinoma
- Head & Neck Squamous Cell Carcinoma
- Lymphoma
- Hepatocellular Carcinoma
- Merkel Cell Carcinoma
- Gastric/Gastroesophageal Adenocarcinoma
- Cervical Carcinoma
- Cutaneous Squamous Cell Carcinoma
- Breast Carcinoma
- Esophageal Carcinoma
- Uterine Carcinoma
- Urothelial Carcinoma
- Genomic Alterations (e.g., MSI-high)

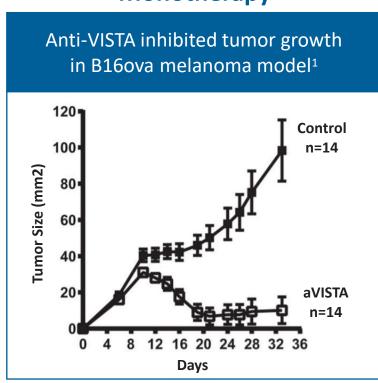
Target V V V **VISTA (CI-8993)** V X PD-1 (Pembro, Nivo, etc.) X X V X X X PD-L1 (Atezo, Durva, etc.) V X X X X CTLA-4 (Ipi) V V X TIM3 X X X X X V LAG3 V X X X X OX40 V X X X X **TIGIT**

CI-8993 Preclinical Data



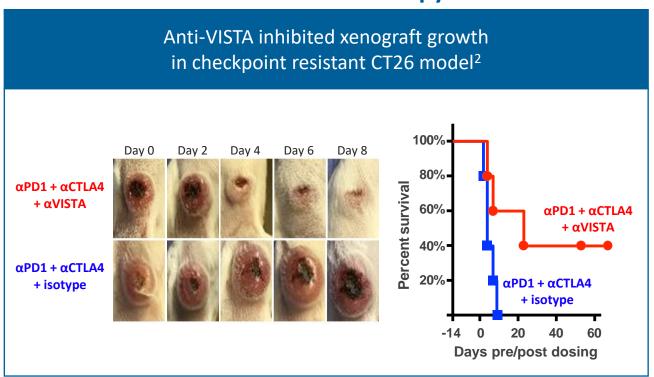
Clear anti-cancer activity suggest potential transformation of immune-oncology treatment

Monotherapy



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

Combination Therapy



² J. Lines, IEBMC Conference 2019

Incorporated Learnings from CI-8993 Prior Clinical Study



Pharmacodynamic activity (cytokine release) observed in initial clinical study

CI-8993 is the first anti-VISTA monoclonal antibody (IgG1k) to be studied in clinical trials

- Janssen initiated a Ph1 study in 2016 and enrolled 12 patients¹
 - Transient Cytokine Release Syndrome (CRS) observed in several patients at 0.15mg/kg
 - Transient grade 3 CRS-associated encephalopathy observed at 0.3mg/kg, after which Janssen halted the study

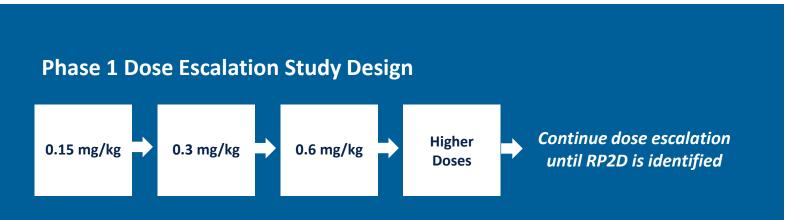
CI-8993 Protocol Designed to Manage Expected CRS

- CRS is likely an on-target effect; indicates drug is hitting the target and inducing immune response
- NCCN guidelines were issued in 2018; oncology community now familiar with managing CRS
- Desensitizing step-dose of CI-8993, and pre/post-infusion medication, administered to mitigate CRS

CI-8993 Clinical Plan: Phase 1 Dose Escalation Study



On-going clinical study to determine safety



Patient Population

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

Treatment

- Bi-weekly dosing
- Plan to mitigate potential toxicities by co-medication and step dosing (desensitization)

Objectives

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

CI-8993 Has Demonstrated Favorable Safety Profile



Successfully managed expected CRS at all levels dosed to date

All Grades Treatment-Related Adverse Events Occurring in 2+ Patients		5 mg/kg (N = 7)	0.3 mg/kg (N = 5)		
		n (%)		n (%)	
Number of patients having any grade treatment-related AEs	4	(57.1)	4	(80.0)	
Headache	3	(42.9)	1	(20.0)	
Chills	2	(28.6)	1	(20.0)	
Alanine aminotransferase increased	1	(14.3)	1	(20.0)	
Fatigue	2	(28.6)	0		
Hypotension	0		2	(40.0)	

Grade 3+ Treatment-Related Adverse Events	0.15 mg/kg (N = 7)		3 mg/kg (N = 5)
	n (%)		n (%)
Number of patients having grade 3+ treatment-related AEs	0	1	(20.0)
Leukopenia	0	1	(20.0)

Data extraction date: Dec 11, 2021.

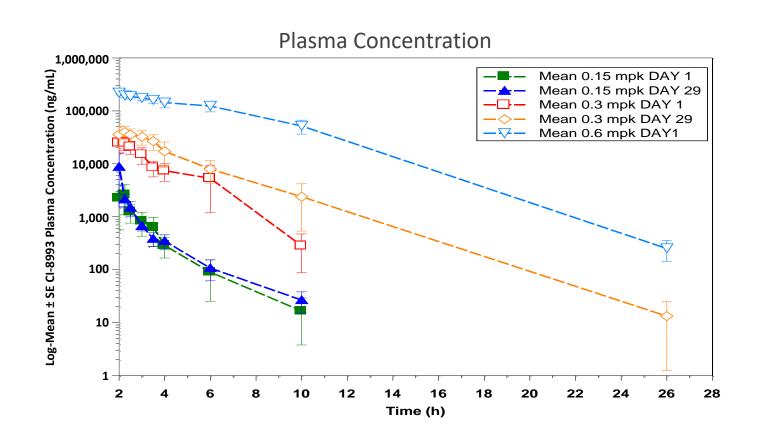
One additional patient experienced grade 2 treatment-related AE after receiving step dose and chose not to proceed to full dose.

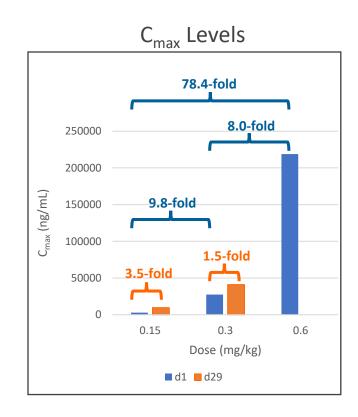
CI-8993 has successfully cleared dose level where Janssen observed DLT

CI-8993 Has Demonstrated Favorable PK Profile



CI-8993 mean plasma concentration vs. time profile following IV administration at full dose



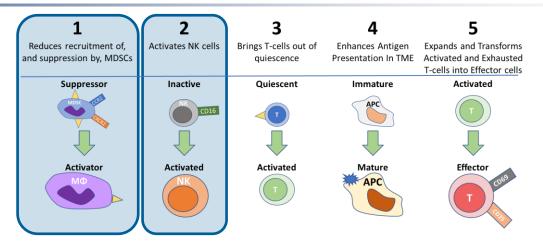


Saturation kinetics in C_{max} data ("sink effect") suggest potential for broad bioavailability at higher dose levels

Pharmacodynamic Effects of CI-8993 in Patients



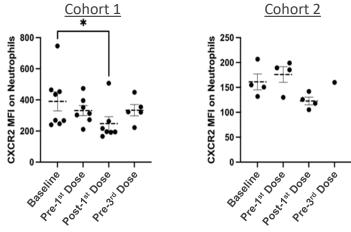
CI-8993 affects multiple anticancer mechanisms supporting VISTA potential



Decreased recruitment of MDSCs

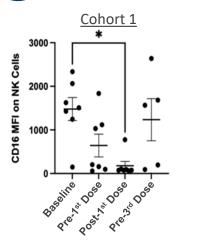
Decreased CXCR2 on granulocytes

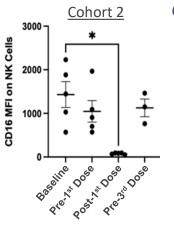
CI-8993 reduces MDSCs
(↓CXCR2 and ↓CCR2);
MDSCs suppress antitumor immunity and
impair efficacy of other
checkpoint inhibitors



Similar finding for CCR2 on monocytes

NK Cell Activation Decreased CD16 on NK cells



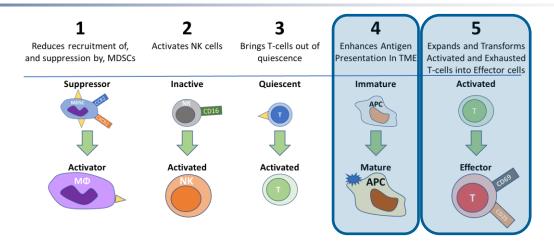


CI-8993 activates NK cells
(↓CD16 signifies NK
activation); activated NK
cells exert an important
anti-tumor function via the
innate immune system

Pharmacodynamic Effects of CI-8993 in Patients



CI-8993 affects multiple anticancer mechanisms supporting VISTA potential

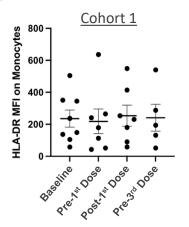


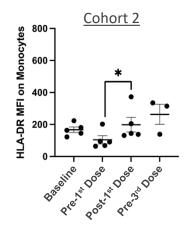
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Enhanced Antigen Presentation

Increased HLA-DR on Monocytes

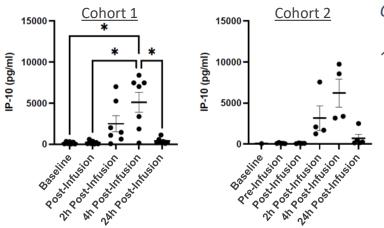
CI-8993 enhances antigen presentation (↑HLA-DR); antigen presentation allows the immune system to recognize the tumor and attack it





Release of T-Cell Activating Factors

Increased Secretion of IP10



CI-8993 increases T-cell factors (↑IP10 and ↑MIP1α); these stimulate T-cell expansion and transformation into effector T-cells

Similar finding for MIP1lpha

CI-8993 Cleared Initial Safety Hurdle



First-in-class CI-8993 has potential for broad applicability in immune checkpoint therapy

- Encouraging initial safety data appears to demonstrate effectiveness of procedures implemented to manage expected CRS
- Pharmacokinetic profile of CI-8993 exhibits saturation kinetics, suggesting potential to overcome "sink effect"
- Pharmacodynamic effects of CI-8993 in patients suggest multiple anti-cancer mechanisms may be activated

Next Steps in Dose Escalation

 Continue dose-escalation for signs of anti-cancer activity and determination of RP2D

Corporate Overview



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 Cash and investments of approximately \$150M as of September 30, 2021; cash runway into 2024
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
Upcoming Milestones	 1H 2022: Discuss potential for rapid approval path for CA-4948 with FDA 1H 2022: Report initial data for CA-4948 in combination with ibrutinib in NHL 2022: Report updated data for CA-4948 in AML/MDS monotherapy 2H 2022: Report initial efficacy data for CI-8993 (VISTA) 2H 2022: Report initial data for CA-4948 in combination with aza or ven in AML/MDS

Curis



Committed, Experienced Leadership Team





















End of Corporate Presentation

NASDAQ: CRIS

